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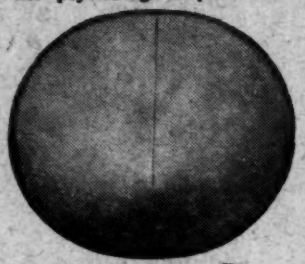

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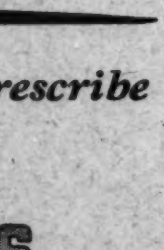

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY JANUARY 19 1952

STREPTOMYCIN IN OPHTHALMOLOGY

BY

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Tuberculous lesions of the eye and infections by Gram-negative bacilli constitute the two groups for which streptomycin therapy would be indicated on theoretical grounds. The cases diagnosed as tuberculous are a composite group. Tubercle bacilli, or typical giant-cell formation, can be demonstrated in tuberculous conjunctivitis, but for the mass of lesions diagnosed as tuberculous keratitis and tuberculous iritis no such definite evidence is generally available. The diagnosis in such cases is usually on clinical grounds, with very variable supporting evidence. As for infections by Gram-negative bacilli, these are on the whole infrequent, the outstanding examples being infection of the cornea by *Pseudomonas pyocyanea* and by *Proteus vulgaris*. Here bacteriological evidence is readily available. Apart from being easily established bacteriologically, the clinical picture that these Gram-negative bacilli give in the cornea is characteristic. Instead of the classical serpiginous corneal ulcer and hypopyon, there is a corneal ulcer with a sloughy base, frequently heaped up, and generally extending as infiltrates well into the surrounding corneal tissue; hypopyon is not a characteristic concomitant, but is not exceptional and is apt to appear very dense. These corneal infections do not respond to the sulphonamides or penicillin, and they run a rapid and disastrous course, often leading to opacification of the whole of the cornea and to perforation.

It is generally accepted that tuberculosis of the conjunctiva, cornea, iris, and retinal veins is secondary to a general infection. This does not exclude local therapy as an agent of some value, but does emphasize that exclusively local therapy is unlikely to prove satisfactory. In the case of infections with Gram-negative bacilli the lesion is exclusively local, and local treatment may therefore be expected to give the desired results.

In the present study an attempt has been made to establish the levels of concentration that can be reached in the eye by the systemic and subconjunctival injection of streptomycin; the efficacy of such administration in experimental infection of the cornea by *Ps. pyocyanea* has been investigated; and we have tried to evaluate the use of streptomycin clinically.

Experimental Studies

(a) Ocular Tolerance of Streptomycin Injected Subconjunctivally

The purified streptomycin salt at present available is soluble to the extent of 0.5 g. in 1 ml. of water. The solution thus obtained is well tolerated by the rabbit when injected subconjunctivally—in fact, very much better than 1,000,000 units of penicillin similarly given.

There is nothing to be gained by giving smaller doses subconjunctivally. Larger doses cannot be given, as more than 0.5 g. does not go into solution in 1 ml.

(b) Levels of Concentrations Reached in the Eye by the Systemic and Subconjunctival Injection of Streptomycin

Method.—Rabbits weighing 2.5–3 kg. were used for the tests. Dihydrostreptomycin sulphate was injected in three ways: (1) 50 mg. per kg. was injected in 2 ml. of physiological saline intramuscularly; (2) 500 mg. was injected in 1 ml. of distilled water subconjunctivally; and (3) 500 mg. was injected in 1 ml. of 1:1,000 adrenaline subconjunctivally. At appropriate times the animals were killed by the intravenous injection of pentobarbitone sodium and the eyes removed. In the case of the animals treated by intramuscular injection, both eyes were taken and treated as one. They were given a rapid rinse in sterile saline and were then immediately dissected. The aqueous humour, vitreous humour, anterior tissues, posterior tissues, and cornea were separated, minced with scissors, and after weighing were extracted with an appropriate amount of *p*H 8 phosphate buffer. Samples of blood were removed from the left ventricle of the animals just before death. The extracts and the blood samples were titrated for streptomycin content by either the capillary-tube method with *Bact. friedländeri* or by plate assay method using *Bacillus subtilis*.

The results are recorded in Table I.

The following points may be noted: (1) Intramuscular injection of 50 mg. per kg. in the rabbit is equivalent to approximately an intramuscular injection of 4 g. in an adult patient—well beyond the toxic limit. With this dose it will be noted that levels at four hours and subsequently are *nil* in the vitreous and cornea, whilst the aqueous gives a level of only 0.3 μg. at four hours. The levels at two hours are also not high. (2) A subconjunctival injection of 500 mg. in 1 ml. of water gives considerable levels in the aqueous and vitreous,

TABLE I.—*Ocular Concentrations of Streptomycin in the Rabbit After Administration by Different Routes*

Route and Dose	Time (hours)	Streptomycin Levels (μg./ml. or μg./g.)					
		Blood	Aqueous	Vitreous	Ant. Tissues	Post. Tissues	Cornea
Intramuscular; 50 mg./kg.	2		1·3	0·5			Trace
	4		0·3	0			0
	6		0	0			0
	8		0	0			0
Subconjunctival: 500 mg. in 1 ml. water	2	254	14·0	7·0	360	230	35·0
			9·5	<2·2			460
	6	9·0	6·0	4·0	6·0	7·5	7·5
			4·0	<1·1			12·5
	12		1·6	1·9			<0·5
	16	0·57	1·44	<0·37	<1·85	<1·85	<3·7
	18		0	0			0
	20	0·26	<0·4	<0·2	<1·0	<1·0	<1·0
	24		0	0			0
Subconjunctival: 500 mg. in 1 ml. 1 : 1,000 adrenaline	2	190	156	190	4,000	3,000	1,575
	4		64				128
	6		<16				25
		17·0	13·5	<2·2	30	38	32
	12	5·3	164	2·3	164	47·5	282
	24		>28				3·5
		1·5	264	15·3	112	30	900
	28		>40				3·3
	36	1·62	87·5	4·53	117	57	283
		<0·37	<0·74	<0·37	3·1	10·25	<1·85
	48	<0·2	<1·0	<1·0	2·15	1·9	<2·0
		<0·2	<0·4	<0·2	3·12	7·0	<1·0

persisting for about 12 hours. (3) A striking feature is the markedly increased initial intraocular concentrations when streptomycin is dissolved in adrenaline 1 : 1,000 instead of water, and the considerably longer persistence of these levels : at 36 hours the levels are still significant.

These findings are of the same order as those recorded for penicillin: subconjunctival injection gives higher levels than intramuscular injection, and the levels become both higher and more persistent when adrenaline is added to the solvent.

(c) Experimental Infection of the Cornea with Ps. pyocyanea

Method.—Thirteen rabbits were used. The cornea of the right eye of each rabbit was scarified with a scalpel blade and infected with two loopfuls (3-mm. diameter loop) of a suspension of *Ps. pyocyanea* (24-hour agar culture of strain 150 E), the suspension being rubbed into the scarified area with the loop for about 15 seconds. Three of the animals were kept as controls. The remaining 10 were treated three hours after infection by the injection, subconjunctivally into the infected eye, of 0.5 g. of dihydrostreptomycin sulphate in 1 ml. of 1:1,000 adrenaline. A single dose only was given. The course of the infection was followed in all of the animals by daily inspection. The heavily infected control animals were killed on the sixth day, when the corneae had perforated.

The results in this experiment are summarized in Table II.

It will be seen that the three control animals all showed the disastrous course characteristic of *Ps. pyocyanea* infection in the rabbit. The 10 animals treated with a single subconjunctival injection of 0.5 g. of streptomycin in adrenaline 1 : 1,000 gave eminently satisfactory results. By the third day only two of these ten had not recovered fully. By the fifth day one of these two had become normal. The damage in the one animal that had not responded fully was almost negligible.

Clinical Experiences

The clinical results recorded here have been collected over the past three years. In the earlier stages purified streptomycin was not available and dosage was hampered by irritative reactions. In all, streptomycin was used systemically or locally in 53 cases, which fall into four clinical groups :

Group I.—Cases with a definite bacteriological or histological diagnosis. These comprised tuberculous conjunctivitis, acute conjunctivitis, dacryocystitis, infected corneal ulcer, and one case of intraocular infection, all due to Gram-negative bacilli or to penicillin-resistant organisms.

Group II.—Cases presumed to be tuberculous on good clinical grounds. This group consisted of three cases of tuberculous keratitis.

Group III.—Cases presumed to be tuberculous on indefinite clinical grounds—Eales's disease, iridocyclitis, and scleromalacia perforans.

Group IV.—Cases of tuberculous allergy—phlyctenular ophthalmia.

Group I. Cases with Definite Histological or Bacteriological Diagnosis

(*a*) *A Case of Tuberculous Conjunctivitis.*—A child aged 5½ had a large sloughing ulcer in the inferior fornix of the left eye; biopsy showed it to be tuberculous, with tuberculous giant-cells and caseation; tubercle bacilli were demonstrated in the smear of the guinea-pig inoculation. Treatment with intramuscular streptomycin, 0.5 g. a day for 30 days, caused rapid resolution of the lesion clinically, but, histologically, cure was much slower. Biopsy three months later showed fibrous tissue with a few epithelioid cells, while guinea-pig inoculation

TABLE II.—*Treatment of Ps. pyocyanea Infections of the Cornea in Rabbits with Dihydrostreptomycin Sulphate in Adrenaline*

Rabbit No.	Treatment	Appearance of Infected Eye after Infection			
		3 Days	5 Days	6 Days	19 Days
1	Control untreated	Leucoma of cornea in 3 mm. diam. zone at site of infection	Mild central opacity with peripheral vascularization. Commencing panophthalmitis	Perforation of cornea. Animal destroyed	
2	,, ,,	Complete opacity of cornea with pus in anterior chamber	Complete corneal opacity with grey infiltration. Useless eye	,, ,,	
3	,, ,,	Complete opacity of cornea with conjunctival and corneal ulcer	Staphylomatous cornea with hypopyon. Useless eye	,, ,,	
4	Treated with 0·5 g. streptomycin in adrenaline	Eye normal	Eye normal. Some slight lid reaction due to streptomycin		Eye normal
5	,, ,,	,, ,,	Eye normal		,, ,,
6	,, ,,	,, ,,	,, ,,		,, ,,
7	,, ,,	,, ,,	,, ,,		,, ,,
8	,, ,,	,, ,,	,, ,,		,, ,,
9	,, ,,	Slight corneal opacity, not at the spot where infected. Slight conjunctivitis with discharge	Very slight corneal haze. Otherwise normal eye		Slight corneal opacity
10	,, ,,	Eye normal	Eye normal		Eye normal
11	,, ,,	,, ,,	,, ,,		,, ,,
12	,, ,,	Very slight corneal opacity. Some lid reaction	,, ,,		,, ,,
13	,, ,,	Eye normal	,, ,,		,, ,,

was negative. When seen recently, 18 months later, there was no sign of the lesion beyond fibrosis, and there had been no relapse.

(*b*) *Six Cases of Acute Conjunctivitis.*—All cases were due to *Proteus vulgaris* except one case, which produced a penicillin-resistant staphylococcus after prolonged local penicillin therapy. Four cases were initially treated by other drugs which had no effect; two cases, in which the smear showed Gram-negative organisms, were started on streptomycin immediately. Two cases were treated with drops (in a concentration of 0.5 g. per ml. instilled at half-hourly intervals), three with ointment (0.1 g. per g.), and one, following a cataract extraction, with subconjunctival streptomycin (0.5 g. in 10 min. (0.6 ml.) of water and 5 min. (0.3 ml.) of adrenaline 1:1,000). All cases cleared up quickly. The results were comparable to those seen with local penicillin therapy in conjunctivitis due to penicillin-sensitive organisms.

(*c*) *A Case of Acute Dacryocystitis.*—This was a severe recurrence of a typical acute dacryocystitis which did not respond to four days of systemic penicillin, in the last two of which the sac was also syringed with penicillin. Systemic streptomycin therapy (0.5 g. a day for five days) led to a rapid and uninterrupted recovery, the sac remaining patent. The organism proved to be *P. vulgaris*.

(*d*) *Nine Cases of Infected Corneal Ulcer.*—Six cases occurred within five days of having had a corneal foreign body; one was an ophthalmia neonatorum; one was a secondary infection of a dendritic ulcer; and one was a case of marginal ulcer of unknown cause. The organisms in these nine cases were *Ps. pyocyanea* in two cases, Gram-negative bacilli in three cases, and *P. vulgaris*, *Bact. coli*, *B. xerosis*, and bacillus of Patel in one case each. All but two cases were given daily subconjunctival injections of 0.5 g. of streptomycin within two or three days of the start of infection; one case had been worsening for three months, and in the other, the baby with ophthalmia neonatorum, treatment by drops and intramuscular injection was started 10 days after onset, there having been very slight improvement on systemic sulphonamide for six days. Two cases had been started on streptomycin immediately, one having been diagnosed as a Gram-negative type of infection clinically and confirmed bacteriologically next day, 24 hours thus being saved; while the other showed Gram-negative bacilli in the smear. Five cases had one dose of subconjunctival penicillin (1,000,000 units) on admission, the nature of the infection not being known till 24 hours later, from the culture. The conjunctiva became friable after repeated subconjunctival injections, and, when it would hold no more, streptomycin was given retrobulbarly. This is probably less effective.

The Subconjunctival Injection.—The dose was at first 1 g. of streptomycin in 2 ml. of fluid, but this has been reduced to 0.5 g. in 1 ml. The solvent used is as for subconjunctival penicillin—a stock solution, 10 min. (0.6 ml.) of which contains 1/40 gr. (1.6 mg.) of atropine sulphate and 1/8 gr. (8 mg.) of cocaine hydrochloride. To 10 min. (0.6 ml.) of this solution is added 5 min. (0.3 ml.) of adrenaline 1:1,000 before injection.

Results.—All cases were left with a quiet eye, except the one which was hopeless to begin with and became quiet only after perforating. Three cases had a poor visual result of 3/60 or less, due to dense corneal scarring owing to the severe initial damage before streptomycin treatment was instituted. The remaining cases obtained a good visual result, the corrected visual acuity being 6/9, 6/12, and 6/12 in three cases, and 6/36 under a mydriatic in a patient who could not be followed up. The baby with ophthalmia neonatorum had a thin residual scar.

(*e*) *A Case of Post-operative Intraocular Infection.*—A man with a right detached retina had a lens extraction for traumatic cataract in the other eye while under systemic penicillin and local treatment to control an intractable otorrhoea. Forty-eight hours after operation subconjunctival streptomycin, 0.5 g., and systemic streptomycin, 0.5 g., were started, as the anterior chamber was infected; treatment was continued for five days. The infection subsided and some useful vision may be expected after needling.

Group II. Cases Presumed to be Tuberculous on Good Clinical Grounds

Three Cases of Tuberculous Keratitis.—Three typical cases with long histories were treated for one or two months with between 2 g. and 0.5 g. of intramuscular streptomycin daily, the dosage tending to decrease while the duration of the course tended to increase. All cases improved markedly within a fortnight, and in one case the result was particularly striking: the visual acuity improved from hand movements in both eyes to 6/60 in the right eye and 6/9 in the left eye—very much better than it had been for years. These three cases have now remained quiet for periods of 10, 19, and 26 months respectively.

Group III. Cases Presumed Tuberculous on Indefinite Clinical Grounds

(*a*) *Four Cases of Eales's Disease.*—Four cases presented as Eales's disease: only one case showed (in a chest radiograph) any further evidence of tuberculosis. These patients were given systemic streptomycin for one or two months, with between 2 g. and 0.5 g. of intramuscular streptomycin daily, the dosage tending to decrease with a longer course. The results are dubious and indefinite. The most that can be claimed is the absence of relapses in three cases which seemed quiet or quiescent at the start, while the one active case has become worse.

(*b*) *Five Cases of Iridocyclitis.*—Four of these five cases had a common history of slowly worsening iridocyclitis for over six months, with the development of mutton-fat K.P., before streptomycin was started; in the remaining patient there was a history for only two months. Two of these cases had further indications of a possible tuberculous origin—tuberculous pleurisy in the one, and a strong family history of tuberculosis in the other. Two patients, both young women, developed retinal vasculitis. All received one dose of streptomycin, 0.5 g. a day for a month intramuscularly, except one patient who had side-effects necessitating its discontinuance after 17 days. One patient has shown only slight improvement, and it is now three months since she had the course; another became completely clear only seven months after the course; two patients who developed secondary glaucoma and pain just before the course had (three months later) normal tension and no pain, and the K.P. had become thinner and crenated. The patient who had had an incomplete course owing to toxic effects now has only a slight aqueous flare in both eyes, but, as she responded to *x*-ray therapy shortly after the streptomycin was discontinued it is impossible to say to which treatment (if to either) her improvement should be attributed.

(*c*) *Iridocyclitis with Nodules.*—Of three cases, one, that of a woman aged 20 with multiple nodules in one iris—the whole reaction strongly suggestive of sarcoidosis—showed no response to systemic administration of streptomycin. The two other cases, with an isolated nodule in each instance, appeared to improve. Steady diminution of the nodule was observed during a month's treatment by intramuscular injections of 0.5 g. daily, but the improvement has not been maintained. In one case the nodule is still as large as before, and in the other there is a recurrent iridocyclitis.

(*d*) *Three Cases of Scleromalacia Perforans.*—These cases, which had been progressing steadily, were given 0.5 g. of streptomycin systemically six-hourly for 28 to 56 days. In none was there any improvement.

Group IV. Cases of Tuberculous Allergy : Phlyctenular Ophthalmia

Children with phlyctenular ophthalmia were found to improve quickly on mydriasis and an open-air regimen at White Oak Hospital. Seventeen cases were given systemic streptomycin in addition, because they either showed no response or relapsed repeatedly. Fourteen cases had active lesions when the course was started—nine for at least two months and five for three weeks or less. Four of these children had long histories of repeated relapses. In addition streptomycin was given to two cases which had shown frequent relapses but were then quiet, and to one case which was almost quiet before the course started.

The diagnosis, made on clinical grounds, was supported in 15 cases by one or more of the following features : positive Mantoux reaction, a positive chest *x*-ray finding, and a family history of tuberculosis.

At first streptomycin was given on a basis of 20 mg. per lb. (0.45 kg.) body weight a day in divided doses for a week, but later in the investigation the amount of the drug was reduced, and it was given in one daily dose over a longer period, the ultimate dosage used being 10 mg. per lb. (0.45 kg.) a day for 56 days.

In the acute case streptomycin proved of value in cutting short the acute attack and possibly also in preventing recurrences. The results in the 14 active cases may be tabulated as follows :

Activity under Control Within	No. of Cases	Relapses Within 3 Months	No. of Cases	Follow-up Results After First 3 Months of 13 Controlled Cases	
				Quiet for	No. of Cases
7 days ..	2	No relapse	5	24–28 months	3
10 ,, ..	5	One ,,	3	18–24 ,,	3
21 ,, ..	4	Two relapses	3	12–18 ,,	3
28 ,, ..	1	Three ,,	2	Relapse: a year later	1
56 ,, ..	1	Uncontrolled	1		
Uncontrolled..	1			Not known—trace lost	3
	14		14		13

The results in the three cases treated during the quiescent stage in the hope of controlling their tendency to frequent relapses were : (1) Frequent recurrences for the 21 months under observation in one case, but the attacks were probably milder. (2) Three relapses in the two months following the course and three more in the four months subsequent to a second course. Since then quiet for 18 months. (3) No relapse for four months after a course of treatment—in contrast to three attacks in two months before treatment.

Discussion

The excellent results achieved with penicillin in infections of the eye due to penicillin-sensitive organisms have thrown into sharp relief those infections, largely due to Gram-negative bacilli, for which penicillin is ineffective Some cases of acute conjunctivitis and acute dacryocystitis are caused by penicillin-insensitive organisms, but the more threatening of the acute lesions is infection of the cornea by Gram-negative bacilli. These run a rapidly destructive course, for the corneal reaction is essentially a proteolytic phenomenon consistent with the proteolytic properties of these organisms.

The recognition of Gram-negative infection of the cornea as a characteristic clinical entity calling for specific treatment appears to have been anticipated by the older literature. The concept of corneal abscess of the older literature does not seem to have been well defined, the term being used for corneal ulceration with diffuse infiltration as well as for interstitial corneal reaction without ulceration. It is likely that what went under the name of corneal abscess included the group of infections of the cornea by Gram-negative bacilli stressed here. In so far as it emphasizes the interstitial reaction of the cornea, that designation was most useful The complete clinical picture appears, however, to require equal stress on the sloughy, heaped-up base of these corneal ulcers.

The experimental evidence from infection with *Ps. pyocyanea* that such infected ulcers respond well to streptomycin is supported by the limited clinical experience reported here, and it may be assumed that with early and adequate streptomycin treatment these corneal infections will respond as readily as serpiginous ulceration responds to penicillin. Whilst the experimental results were obtained with 1 ml. of adrenaline as the solvent, clinically it would not be safe to use so much adrenaline. For this reason it would be best to use 10 min. (0.6 ml.) of water and 5 min. (0.3 ml.) of adrenaline. The solvent can readily be adjusted to give a mydriatic effect by incorporating 1/8 gr. (8 mg.) of cocaine hydrochloride and 1/40 gr. (1.6 mg.) of atropine sulphate in the 10 min. (0.6 ml.) of water. A stock solution containing these ingredients is easily prepared, and keeps well, but it is essential that the adrenaline should not be added to the solvent until use.

The value of streptomycin in the tuberculous infections of the eye is not so definite, if only because diagnosis is frequently uncertain. Judging by the proved case of tuberculous conjunctivitis recorded here, as also by the cases of presumed tuberculous keratitis, systemic treatment is of considerable help. Whether these cases should not in addition be treated by local applications is an open question. The results in phlyctenular ophthalmia are also hopeful. Here there seems less reason for local treatment. The disappointing results obtained in plastic and nodular iritis, presumed to be tuberculous in origin, and in Eales's disease, may arise from inadequate use of streptomycin or from a fallacious aetiological interpretation.

Summary

Streptomycin, 0.5 g. in 1 ml. of water, is well tolerated on subconjunctival injection.

Such doses give considerably higher intraocular levels when injected subconjunctivally than on intramuscular injection.

The intraocular levels are higher still and persist up to 36 hours if adrenaline 1:1,000 is the solvent.

In the experimental animal a destructive *Ps. pyocyanea* infection of the cornea is fully controlled by one subconjunctival injection of 0.5 g. of streptomycin in 1 ml. of adrenaline 1:1,000.

For clinical purposes streptomycin to be injected subconjunctivally should be dissolved in 10 min. (0.6 ml.) of water to which 5 min. (0.3 ml.) of adrenaline 1:1,000 is freshly added.

Clinically, streptomycin is effective when used subconjunctivally in infections of the cornea due to Gram-negative bacilli. As these lesions are highly destructive, early treatment is essential, and the characteristic clinical appearance of such infections facilitates early diagnosis. Streptomycin locally is also invaluable in acute conjunctivitis due to Gram-negative bacilli.

Systemic streptomycin therapy has proved helpful in tuberculous keratitis. It has given poor results in presumably tuberculous iridocyclitis and in periphlebitis. In phlyctenular ophthalmia it tends to cut short severe attacks, and probably reduces the frequency and severity of relapses.

Our thanks are due to Dr. P. D'Arcy Hart and the Medical Research Council for liberal supplies of streptomycin during the earlier stages of this investigation, when the material was not readily available. We are obliged to Sister Thorogood and her staff of the Royal Eye Hospital unit at Lambeth Hospital and to Sister Condon, formerly of White Oak Hospital, for their help in the treatment of patients. To Dr. P. Muggleton and Mr. B. I. Helliwell, of Glaxo Research Laboratories, we are indebted for technical assistance.

THE CLINICAL FEATURES OF THE PNEUMONIAS UNDERGOING VIRUS TESTS

BY

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The response of the pneumonias to sulphonamides and penicillin has broadened rather than solved the problem of the differential diagnosis and treatment of lung consolidations. Since such treatment has been introduced, a wide group of non-bacterial pneumonias caused by viruses and rickettsias has been revealed. American authorities have stressed the increasing incidence of virus pneumonias, Goodrich and Bradford (1942) finding them almost as frequent as pneumococcal pneumonias, and Reimann (1943) computed figures of 70% of all pneumonias for this group. The process of sorting out the various non-bacterial pneumonias is not yet far advanced, and while influenzal pneumonias and the pneumonias of psittacosis, lymphocytic choriomeningitis, glandular fever, lymphogranuloma venereum, and Q fever have emerged as definite entities other similar pneumonias await identification.

The group of "primary atypical pneumonia, aetiology unknown," has been considered by some as an entity (Joules, 1950), but this has been denied elsewhere (Scadding, 1948). In the last-named condition the non-specific cold agglutination reaction has been used as a diagnostic test; in the other pneumonias mentioned the diagnosis is confirmed by the detection of specific antibodies by complement-fixation and neutralization tests. A rise in antibody titre in these tests is diagnostic and is particularly valuable in influenza, in which it is often impossible to obtain the virus from the patient's nose or throat and so to isolate it by ferret inoculation.

The complement-fixation test was the one employed in the series of cases described below, and most of the cases were also examined for complement-fixing antibodies of *Rickettsia burneti*, psittacosis-ornithosis and lymphogranuloma viruses, and by *Streptococcus M.G.* agglutination. Where possible the tests were done on acute and convalescent phase sera, but in some cases only convalescent sera were obtainable. These tests were performed by Dr. B. P. Marmion, Dr. A. D. Macrae, and Dr. A. P. Goffe, of the Colindale Group Laboratory. Cold haemagglutination tests were also done on many of the cases at the Edgware General Hospital by Dr. E. D. Hoare. Nearly every case was questioned and examined by me so as to obtain a uniform approach to the clinical aspects of these cases of pneumonia. This paper is a review of the clinical findings in 159 of such cases seen in the Edgware General Hospital between the beginning of January, 1949, and the end of May, 1950.

Clinical Investigation

It soon became apparent that clinical methods did not readily distinguish the various forms of pneumonia, so *all* cases of suspected lung consolidation seen during the investigation were serologically tested. The cases are divided into two groups, the first being seen between January 1 and September 1, 1949, and the second group between early November, 1949, and the end of May, 1950. A fairly severe outbreak of influenza (mainly of the A type) is included in the first group, and the second group covers a lesser outbreak of influenza B in March and April, 1950. While the patients were being submitted to the tests just mentioned special consideration was also given to certain features: the history and symptoms of the illness; a past history of chest infection; the signs of the illness; the duration of the fever; the *x*-ray findings; the white cell counts; the sputum examinations; and the nature of any complications.

The two groups showed very similar numbers of cases. 88 being examined in the 1949 group, and 71 in the 1949–50 group. The cases were all of severe respiratory disorder, and either showed clear pneumonic signs or had such symptoms of lung involvement that pneumonia was immediately suspected. The patients had all been active till the onset of the illness, even though some had old respiratory or cardiac disease, and the rapid development of severe symptoms, often of sudden onset, was a feature in all. The composition of the two groups as determined by the special tests is shown in Table I, the

TABLE I

	Group 1 (1949)	Group 2 (1949–50)
Influenza (confirmed)	16	18
" (probable)	22	—
Primary atypical pneumonia ..	11	11
Psittacosis-ornithosis	—	2
Unclassified	39	40
Total	88	71

"primary atypical pneumonias" being the cases in which a cold agglutinin titre of 1 in 16 or over was reached. The cases classified as definitely positive influenzas were those which showed a rise of influenza antibody titre between the acute and convalescent phases; if a signifi-

cantly high titre was found only in the convalescent phase the case was listed as "probable positive." Neither of the psittacosis-ornithosis cases appeared to have been exposed to avian infection. No case of Q fever was detected during the whole investigation.

The age distribution in the two groups is shown in Table II, and a remarkable similarity is noticeable. Thus

TABLE II.—*Age Distribution*

Age Groups (Years)	Group 1					Group 2		
	Infl. (Confirmed)	Prob. Infl.	Total Infl.	Primary Atypical Pneumonia	Uncl.	Infl.	Primary Atypical Pneumonia	Uncl.
0– 9 ..	1	1	2	0	2	0	0	1
10–19 ..	1	5	6	1	2	0	0	3
20–29 ..	1	1	2	3	2	2	2	4
30–39 ..	3	0	3	2	7	3	3	5
40–49 ..	3	5	8	3	4	4	3	4
50–59 ..	6	5	11	1	10	2	1	13
60–69 ..	1	4	5	0	8	7	1	9
70+ ..	0	1	1	1	4	0	1	1
Totals	16	22	38	11	39	18	11	40

25 (65.8%) of the influenza cases of group 1 were over 40, and 13 (72.2%) of those in the second group were over 40. Of the unclassified cases 26 (66.6%) in group 1 and 27 (67.5%) in group 2 came in this age category. The primary atypical cases were fewer and also on the average younger than those in the other groups; thus 8 (72.7%) in each group were between 20 and 50. The influenza figures correspond with the observations of Stuart-Harris *et al.* (1950) on influenzal cases in Sheffield, many of his cases being in the older age groups.

During the investigation five patients died in group 1 and three in group 2. These figures, which are a striking testimonial to modern treatment, become even more remarkable when the ages of the patients and other associated conditions are considered. Thus in group 1 four patients with "probable" influenza (high complement-fixation titre at the only reading available) died; one of these was 75 and another 60; the third had a contracted horseshoe kidney and uraemia; and the fourth, a boy of 12, an old case of poliomyelitis, had widely paralysed respiratory muscles. One unclassified patient aged 63 died during the first half of the investigation. Of the three fatal cases in group 2 one aged 68 had probable psittacosis-ornithosis; another, a chronic bronchitic with emphysema, aged 52, had a suprarenal haemorrhage, and the third was admitted after six weeks' illness with organizing suppurative pneumonitis.

During the influenza B epidemic period four serologically uninvestigated patients (not included in Table I) died within a few hours of their admission, and three of them, aged respectively 21, 46, and 65 years, had sudden illnesses of influenzal type. All three failed to show influenza virus from lung culture on fertile hen's egg, but all showed a free growth of *Staph. aureus*—a possibly significant finding. The husband of the youngest of these was said to have had influenza a short time previously. The fourth, aged 69, proved to be a long-standing chronic bronchitic with a large area of grey hepatization. Thus among 159 patients with pneumonia who lived long enough to have some treatment and investigation there were eight deaths, usually facilitated by some disease other than the pneumonia, and there were four other deaths of patients in whose case there was no time for effective therapy.

Onset

A comparison between the influenzal cases and the various non-influenzal cases was attempted on the lines mentioned above. Stuart-Harris *et al.* (1938) had underlined the significance of a sudden onset as a feature of the influenzal infections; but in our investigation, which was mainly concerned with ill pneumonic cases, it was possible that this feature might be somewhat obscured. The figures given in Table III, however, show that this

TABLE III

	Sudden Onset	Possibly Sudden	Gradual
Group 1:			
Influenza	14	2*	0
Probable influenza	17	3	2
Primary atypical pneumonia ..	6	2	3
Unclassified	15	5	19
Group 2:			
Influenza	11	3	4
Primary atypical pneumonia ..	7	1	3
Unclassified	13	5	22
Psittacosis	1	0	1

* Both bronchitic cases.

observation holds good, particularly amongst the influenzal cases of group 1. (These were mainly due to the A type of infection, only six B type infections being found.) Only in two of the "probable" cases of this year did the illness appear to have a gradual onset, and in one of these, a girl of 21, recent tuberculosis was also found; the other was an old bronchitic case. Many of this first series were admitted within a week of the onset of the illness. All the cases in group 2 found to be influenzal were of the B type; they were admitted on the average later in the illness, but, even so, only four had symptoms of seemingly gradual onset, and of these one was a case of gross mitral stenosis and two had illnesses of two and six weeks' duration. Thus in only one of the four was the true onset of the infection clearly discernible.

But sudden onset is not confined to influenzal pneumonias, as is clearly shown in Table III. It is noteworthy that over one-third of the "negative" unclassified cases in the two years should have had onsets very difficult to distinguish from influenza. This finding is one of those which encourage the belief that there are other respiratory viral infections yet to be identified. Of the two psittacosis-ornithosis cases the more strongly positive also showed a sudden onset.

Severe headache is regarded as a distinguishing feature of "primary atypical pneumonia," but only half our cases in this group showed this symptom, while headaches of varying severity were seen in just over a quarter of the influenzal and in nearly a third of the unclassified cases.

The frequent occurrence of two phases of onset of the illness is also remarkable in all the groups of cases, 28 of the 1949 cases and 27 of the 1949–50 cases showing this feature. In them, after a beginning usually "influenzal" and sudden, there was a period of malaise followed by partial improvement; then, sometimes after the patient had been active, the illness returned with redoubled force and usually with symptoms suggestive of lung involvement, such as chest pain, dyspnoea, and severe cough. The interval between the two phases ranged from two days to three weeks, but in many cases was about one week. The average length of the interval

was slightly more in the unclassified cases (ten days) than in the influenzal and primary atypical pneumonic cases (seven or eight days). The expected evidence of a bacterial invasion to account for the second phase was not forthcoming in more than two-thirds of these cases, and in them the progressing invasion by the viruses, facilitated by inadequate rest, probably explains the advance of infection.

It is also noteworthy that no influenza-positive case showed cold agglutinins and no case with cold agglutinins showed a positive influenza complement-fixation reaction.

Respiratory Symptoms

Stuart-Harris *et al.* (1938) also emphasized the greater preponderance of malaise and general symptoms over respiratory symptoms in the influenzal cases, though he also seemed to imply that coryzal and non-exudative pharyngitis were common features in influenza. But we found pharyngitis in only 5 to 10% and coryza in less than 20% of all our cases, and laryngitis was conspicuous by its absence. The fact that the cases had usually passed to a pulmonary phase in the disease, and that mental hebetude may have caused some of the patients to forget such early symptoms, does not account entirely for the lack of prominence of these symptoms. On the other hand, our influenzal pneumonias were like those of Scadding (1937) in not being prominently dyspnoeic—except in the rare fulminating cases—but they often showed light cyanosis and a very great deal of toxic apathy and asthenia. And the non-influenzal cases in many instances gave a clinical picture indistinguishable from this.

Before considering the other respiratory symptoms, the effect of preceding respiratory disorders in these cases cannot be overlooked. Thus an old bronchitic case developing influenza naturally soon tended to show an exacerbation of bronchitic symptoms, while an asthmatic was liable to show in addition marked bronchial spasm and wheezing. In such cases dyspnoea was often severe and cyanosis pronounced, and in them the sudden type of onset was less in evidence. The proportion of cases with preceding chronic bronchitis was as great amongst the influenzal cases during the two outbreaks as amongst the other pneumonic cases investigated. The only group in which chronic bronchitis was not a marked feature was the "primary atypical pneumonic" group, and, as has already been pointed out, the average age was lower in this group than in the others. Pleuritic pain was an early feature in from one-half to two-thirds of the cases in each category.

Generally speaking, the symptoms failed to distinguish the influenzal cases from non-influenzal pneumonic cases, an observation in line with those of Francis (1941) and other observers in the United States (Horsfall *et al.*, 1940; Sulkin *et al.*, 1941). Dingle and Abernethy and their co-workers (1948) in the U.S. Commission on Respiratory Diseases worked in two U.S. Army camps and failed to distinguish influenzal cases from other acute respiratory diseases by ordinary clinical methods. While they found sore throat and sputum commoner earlier symptoms in acute respiratory diseases, and sudden onset, muscular achings, and prostration commoner in influenza, such differences were not consistent enough to permit a clear separation. A survey of the results of our case symptoms showed that despite treatment there was a greater tendency to prolonged fever of over one week in the influenzal and "primary atypical pneumonic" cases. As all cases on admission were given full therapy with sulphonamides, and often with penicillin as well, and as resistant bacteria were rarely encountered, this tendency to prolonged fever may in these cases well have been a sign of viral infection.

Analysis of Physical Signs

Before making a comparison of physical signs in the two groups it is interesting to recall the old anatomical division of pneumonias into bronchopneumonias and lobar pneumonias. If an influenzal outbreak occurs the affected cases are likely to be further infected with the prevailing bacteria of the locality, and if these are pneumococci, lobar pneumonic manifestations are likely to be frequent. While a pure pneumococcal lobar pneumonia was once of apparently common occurrence, this is not so to-day, and in our series of 159 cases only one case without evidence of recent viral infection fulfilled all the criteria of lobar pneumonia as regards history, signs, radiological appearance, leucocytosis, and pneumococcal sputum. It is not improbable that pneumococci have been rendered less pathogenic and less widespread by the effective therapy of recent years, but it is also probable that "lobar pneumonias" could on past occasions have been viral pneumonias secondarily infected by pneumococci.

In our cases of the first group seven of those which were an established recent infection with influenza and ten with a probable recent infection showed large areas of dullness, bronchial breath sounds, and rales, and so might have been classified as lobar pneumonia. The signs were unilateral or bilateral and were usually basal; similar findings were made in 15—a similar proportion—of the unclassified cases. The findings in the second group of cases were very similar, and in both years there was one influenzal case in which the lung consolidation had broken down under the influence of *Staph. aureus* and had produced cavernous signs, apical in one instance and basal in another. Scadding (1937) has mentioned the cases in which the dullness to percussion is associated with an absence of breath sounds sufficient to suggest fluid. These cases were fewer in the Edgware series: only one among the influenzas, three among the probable influenzas, and seven among the unclassified cases. In a small proportion of these early cases pleural fluid, usually in small quantities, was actually present, but more usually it appeared later, masking previous typical pneumonic signs.

Scadding has also commented on a stage of influenzal lung infection where patches of slight percussion impairment, weak breath sounds, and adventitia unassociated with *x*-ray changes are found. In these he considers lung oedema to be present, and of those in group 1 we found nine among the established and probable influenzas—one cold-agglutinin positive and eight among the unclassified cases. Nine of the influenzal cases (including the "probables") and ten of the unclassified cases in group 1 showed merely bronchitic signs, unilateral or bilateral rales or rhonchi, or both, without percussion impairment. These cases included a number of chronic bronchitics, but it also must be emphasized that radiological evidence of consolidation occurred more often than could be elicited by physical signs.

The figures for group 2 were largely similar in all instances, and it is evident that influenzal cases cannot be separated from non-influenzal by mere consideration of physical signs.

Scadding (1937) has classified the lung involvement in influenzal pneumonia as follows: (*a*) Cases without clinical signs of lung involvement; (*b*) cases with lung signs but without consolidation; and (*c*) cases with demonstrable consolidation. The last two groups he has further subdivided according to their extent and severity. By use of his criteria, and making allowance for the presence of a number of borderline cases, the extent of lung involvement in our cases is shown in Table IV. It should be explained that, whereas C1 and C2 represent respectively consolidation and more extensive consolidation of patchy nature, C3 cases are those with much bronchitis as well as lobar consolidation, and C4 are cases of purely lobar type.

Table IV further shows the impossibility of separating the cases of the various categories on the basis of clinical signs. As will be seen, this difficulty extends to the so-

TABLE IV.—*Extent of Lung Involvement (Scadding's Classification)*

	1949				1949–50		
	Infl.	Prob. Infl.	Cold Agglut. Positive	Unclassified	Infl.	Cold Agglut. Positive	Unclassified
A ..	0	0	1	1	0	0	0
B1 ..	1	1	0	1	1	1	3
B2 ..	6	3	1	8	3	0	7
C1 ..	6	12	7	21	9	10	19
C2 ..	3	6	2	6	5	0	10
C3 ..	0	0	0	0	0	0	0
C4 ..	0	0	0	2	0	0	1
	16	22	11	39	18	11	40

called primary atypical pneumonias, though, as often noted in the past, these tended to show signs disproportionately small for the amount of consolidation. They also twice showed an extrapulmonary feature peculiar to them in this investigation—namely, conjunctival injection.

An approximate correlation of the physical signs with the radiological findings is discussed in the next section.

Radiological Appearances Correlated with Physical Signs

In all groups these varied greatly, and it can be said at the outset that they did not have any conclusive power in separating cases in the various groups. As might have been expected, prominent bronchial shadows of a linear and branching type were a feature of the bronchitic cases (B1 and B2 of Scadding's classification). A closer-knit reticulation and a very fine mottling in the more affected areas—often basal—was the next degree. These cases and the more definite pneumonias with larger areas of mottling (C1 of Scadding) usually produced a variable degree of percussion-note change with weakened breath sounds and rales at one or both bases. The reticular and mottled appearances were found in all classes of the pneumonias investigated.

A curious dense haze in the lungs, sometimes referred to as a "ground-glass" shadow or "partial" consolidation, was also seen in cases in all groups. The bronchial markings could often be seen through it, and even when extensive it usually spared the lung periphery. There was often with it a history strongly suggestive of viral pneumonia, and it occurred noticeably in the "primary atypical pneumonia" series. The signs were often those of moderate percussion-note change, distant tubular breath sounds, and fine rales, but, like all the other radiological appearances of pneumonia, this partial consolidation was associated with variable signs, the breath sounds over it being sometimes much diminished, at times frankly bronchial, and at others a patchy mixture of the two. The same range of signs was noted both where there were large woolly, partly confluent areas, and also where the consolidation was fully confluent and dense. For example, in one of the "primary atypical pneumonias" a comparable partly confluent consolidation in one lower lobe was associated with bronchial breath sounds and in the other lower lobe with very weak breath sounds.

Where there was marked percussion impairment the *x*-ray shadows were usually dense, but smaller shadows were found in resonant zones, particularly where emphysema had a masking effect. Many cases with chest pain showed pleural friction, and a number of these went on to develop pleural effusions, usually small, clear, and sterile. Pleural effusions always showed typical signs, but these at times suggested rather more fluid than was present—a not surprising fact when one remembered that in other cases consolidation mimicked the presence of fluid.

Two influenzal cases which developed staphylococcal abscesses in the consolidated areas showed clear cavernous breath sounds in the dull area near the cavitation. One non-influenzal case with an abscess cavity associated with little consolidation of the near-by lung showed the usual paucity of signs manifested by lung abscesses.

The slowness with which severe influenzal pneumonias cleared has been previously mentioned, and our cases were no exception. One extensive case took almost five months to become clear, and periods of two months from the outset were not uncommon. The heavy consolidations were naturally the most persistent; the "ground-glass" shadows usually cleared within three weeks, and the fine mottling even more rapidly.

Our findings accord with those of Ackermann (1941), who did not observe any specific form of influenzal consolidation. He found lobular consolidations, peribronchial consolidations, and "miliary" consolidations all in varying combinations. He also found that the appearances suggested pulmonary tuberculosis in some of his cases; but, apart from one case actually complicated by pulmonary tuberculosis and another with small upper-zone abscess cavities, this difficulty did not arise in our cases. The consolidations were usually in the lower zones, and as the shadows were of such varied character tuberculosis was not strongly suggested.

Bacteriology and Blood Examinations

Investigations of the sputum and blood are considered in the same section because a relationship between them might be expected. Scadding (1937) has mentioned that as a general rule his groups A and B (influenzal pharyngitis, tracheitis, laryngitis, and bronchitis) show neither significant organisms nor initial leucocytosis, and he believed that when leucocytosis occurs later in group B it is probably due to secondary infection. Similarly, he considered that in his group C the consolidations were due to secondary invaders which also caused leucocytosis, and in his "lobar" groups C3 and C4 pneumococci predominated in every case.

The question whether influenza or other respiratory viruses can alone cause consolidation is not fully decided. Goodpasture (1919) has described two cases of probable

pure influenzal pneumonia, but the main bulk of the consolidations seen are due to secondary invaders. Scadding refers to the basal pulmonary oedema and alveolitis which occurs when the virus passes into and beyond the terminal bronchioles, but implies that such involvement produces no striking consolidation.

Our cases were admitted usually with at least several days' history of illness and were investigated because of symptoms or signs that were frankly pneumonic; only a few of them had received sulphonamides or penicillin before admission, but all subsequently received one or both of these treatments to lessen the effects of secondary invaders. The first sputum results were therefore rarely modified by treatment. The initial leucocyte counts were considered in relationship to the bacteria of the sputum, to the patient's age, to the duration of the illness, and to a rough assessment of the amount of consolidation in the various groups.

The great majority of cases in all the groups showed some consolidation, but many had no sputum, the coughs being occasional, dry, and harsh, and this lack of sputum was not to be accounted for by treatment before admission. It seemed that in all groups there were those who had no marked bacterial infection, and it is thus not unreasonable to suggest that quite often the suspicion of a largely viral infection of the lungs was supported. Very rarely a patient was too weak to expectorate, and one influenzal patient without sputum who later developed an empyema was such a case. Among the cases with previous chest infections there was, as might be expected, a very large proportion in all groups with a bacterial sputum.

Where the probability of virus participation was great—namely, in those cases with positive influenza complement-fixation or positive cold agglutination reactions—certain facts emerged. Only 9 of the 22 cases of the latter type ("primary atypical pneumonia") showed some evidence of secondary infection, and of these only three showed much consolidation—one of these a very old subject, another a chronic bronchitic, and the third having a heavy *Staph. aureus* infection. But of the influenzal cases, probable and confirmed together, 29 of the 56 had purulent or mucopurulent sputum, and four of the others died before sputum could be obtained.

TABLE V.—*Incidence of Bacillary Infection in the Various Groups*

Infecting Organism, Alone or Mixed	1949			1949–50		
	Infl.	Cold Agglut. Positive	Uncl.	Infl.	Cold Agglut. Positive	Uncl.
Staph. aureus	7	0	3	4	1	2
Pneumococci	5	0	7	4	1	6
Haem. str.	2	1	1	1	0	3
H influenzae	0	0	1	1	0	2
Bact. coli and *Proteus vulgaris*	1	0	3	1	0	0
M.U.R.F.* (including *Str. viridans*) ..	6	3	5	3	3	6
Total cases in group	38	11	39	18	11	40

* Normal mixed upper respiratory organisms in pus-containing sputum and unmixed with other organisms listed.

As can be seen from Table V, *Staph. aureus* was found alone or in mixed infections in the sputum of 11 of the influenza cases; in 7 this was a heavy infection. Among these cases were the severest influenzal pneumonias, with most consolidation, two showing abscess formation. As against this, *Staph. aureus* was found in only 5 of the 79 unclassified cases, while pneumococci were found only 9 times among the influenzas and as many as 13 times among the unclassified groups. Two other cases of probable fulminating influenzal pneumonia in which death occurred soon after admission showed heavy *Staph. aureus* infection, and the predilection of *Staph. aureus* for influenzal pneumonias (Wollenman and Finland, 1943; Stuart-Harris *et al.*, 1950) is thus confirmed to some extent in our cases. Blood occurred in the sputum in these cases only with heavy secondary infections. There were many cases tested (26 in all) in which *Streptococcus viridans* alone or together with *Micrococcus catarrhalis* (M.U.R.F., or mixed upper respiratory flora) were predominant in purulent or mucopurulent sputa. It may be that these organisms can become pathogenic where previous damage has been inflicted on the respiratory tract by virus infection.

The initial leucocyte counts seemed to bear little general relationship to the nature or extent of the infection, to the patient's age, or to the previous duration of the illness. The one partial exception to this fact is found amongst the influenzal cases in which a greater degree of consolidation did correspond in a number to a greater leucocytosis and apparently also, as Scadding (1937) has observed, to appreciable secondary infection of the lung. There was also a general tendency for the cases with little or no consolidation or secondary infection to be the cases without leucocytosis. But even here there are exceptions—for example, one case of *Staph. aureus* infection with lung abscesses whose white cell count was only 6,000. It was evident that the individual variation to infection, so well seen in the general appearance and reactions of patients, extends to the leucocyte counts, and it is evident that, while greater in bacterial diseases, this variation also occurs in viral infections, there extending from moderate leucopenia to moderate leucocytosis. It is thus not surprising that where these two types of infection are associated, as in so many of our cases, the leucocyte count is not a reliable guide to the nature of the pneumonia under consideration.

Complications

As the aim of this paper has been to evaluate the clinical approach to the pneumonias as an aid to distinguishing between the various types, the complications are also considered in this light. The commonest complication is the pleural effusion, and here no great difference between the influenzas and the unclassified groups was found, though the effusion was less common in the cold-agglutinin-positive cases. Only one empyema occurred in the whole 159 cases, and that, in an influenzal patient, contained sterile pus—a striking testimony to the efficacy of penicillin and the sulphonamides. There were in all 24 clear sterile pleural effusions. No cases of incomplete resolution were detected among all the cases who recovered. One only—that with the upper zone abscesses—showed a little residual fibrosis. As already mentioned, one case first showed an acute tuberculous focus during influenzal pneumonia.

A possible point of distinction between cases in the cold-agglutinin-positive group and those in the other groups is the occasional occurrence of severe haemolytic anaemia amongst the former. The case with the highest recorded titre of cold agglutinins (1 in 2,048) showed the

most marked haemolysis, the haemoglobin falling from 70% to 40% in eight days, the red blood cells being uncountable during this period, when slight icterus developed. But there was no correlation between the agglutinin titre and the degree of haemolysis, one case with a titre of 1 in 256 showing a fall of haemoglobin level to 60% (Haldane), though no anaemia developed in others with a similar titre seen at the same time of year. Two other cases with titres of 1 in 32 and 1 in 256 showed haemoglobin levels of 68% and 74%, but an emphysematous subject with a titre of 1 in 1,024 showed no apparent anaemia. The severely anaemic case first mentioned showed a fall of titre to 1 in 128 by the 39th day of her illness. At the end of the seventh week her haemoglobin level was 94% and the red cell count 4,740,000 per c.mm. Of the 137 cases in the other groups only two showed anaemia, and one of these was a toxic influenza B pneumonia with heavy secondary infection with *Staph. aureus*; in this case the haemoglobin level fell at first to 60%, but was back to 90% four weeks later. The other case was that of a patient with severe bronchitis and marked "influenzal" symptoms in whom all influenza complement-fixation tests and cold-agglutination tests were negative.

Stuart-Harris *et al.* (1938) have doubted the liability of influenzal cases to nervous complications, but Hollander (1947) has described 23 cases of post-influenzal "sensory polyneuritis," and Laha and Mitter (1945) have described a case of transient flaccid paralysis of the lower limbs which they attributed to influenza. In neither of these investigations was the diagnosis of influenza serologically verified. Nor does Leigh (1946) claim more for his two cases of polyneuritis than that they occurred during an influenza B epidemic and that some of them had respiratory symptoms. Holmes (1947) described six cases of viral pneumonia possibly of primary atypical type which showed evidence variously of infective polyneuritis, lymphocytic meningitis, and encephalitis.

One of our established influenza A cases, a girl aged 10 with slight basal pneumonia, showed immediate neck rigidity and a positive Kernig's sign; her cerebrospinal fluid (C.S.F.) at first contained 30 lymphocytes per c.mm. Her influenza antibody titre rose from less than 1 in 4 on the third day of the illness to 1 in 64 on the 21st day. Another probable influenza A case (titre 1 in 128) showed exaggerated tendon-jerks in the legs and one indefinite and definite extensor plantar response for a few days early in the illness. Two cases showed symptoms of polyneuritis of the greatest severity. One of these was a woman of 56 with probable influenza A (titre 1 in 16), the other, a man of 41, had a primary atypical pneumonia (cold-agglutinin titre 1 in 64). The former, who had complete ophthalmoplegia and incoordination of the arms and legs, also showed marked general flaccid paralysis of the face and moderate flaccid weakness in all four limbs, with slight peripheral sensory loss in all four limbs. Tendon-jerks were persistently absent. C.S.F. protein was raised to 90 mg. per 100 ml., with normal cytology. Over a period of five months she made an almost full recovery. The man was less severely affected, but had complete bilateral facial palsy and a severe flaccid paralysis of both lower limbs with loss of tendon-jerks and slight sensory loss. C.S.F. protein was 270 mg. per 100 ml.; cytology was normal. Limb power recovered well, and he was able to leave hospital walking after two months, but the facial weakness has been very persistent.

Discussion

This account is more concerned with diagnostic than with therapeutic problems, and because "aureomycin" and chloramphenicol were not easily available throughout a great part of the period of observation they were not tried. Despite this, out of 159 cases of severe respiratory disease, mainly pneumonic and often in subjects past the prime of life, only eight (5%) died. Only in this 5% group where the dice were very heavily loaded against recovery did the sulphonamides, penicillin, oxygen, and good nursing fail to cure. In all other cases there was recovery without noticeable residuum, and only one recovery was delayed by the formation of an empyema. Secondary invasion with bacteria, and particularly with *Staph. aureus*, was seen both in the observations in this paper and elsewhere (Wollenman and Finland, 1943) to be the main cause of complications and death in viral pneumonias. This fact is well attested by the efficacy of the remedies just mentioned both in prophylaxis and in curative therapy. The liability to secondary infection seemed less marked in "primary atypical pneumonias" than in the influenzal groups, but, even so, the former tended to have a fairly prolonged febrile course, which newer antibiotics might well have curtailed.

It is evident that the viral pneumonias are still a largely uncharted country for these groups of cases, which were tested for various viruses yet showed at the last a majority of unclassified cases without significant bacterial infection. It is also evident from the uniformity of the clinical findings within the various groups that only with the help of the virus expert, and the wider employment of complement-fixation tests such as those for influenza and other virus infections used during this investigation, will the whole obscure problem be elucidated.

Summary

During 1949 and 1950 one observer saw 159 cases of pneumonia, many of them with symptoms suggestive of virus infection. They have been examined from the clinical, radiological, and viral aspects.

The virus tests have separated a group of influenza A cases and a few influenza B cases in one year, and a number of influenza B cases in the second year. These cases could not certainly have been detected by any other means, although their occurrence during influenza epidemics made them especially suspect. Their tendency to be secondarily infected with *Staph. aureus* was once again evident. Other probable cases of viral pneumonia indistinguishable from the influenza cases in symptoms, signs, *x*-ray appearances, blood counts, and bacteriology were seen during the epidemics and at other times.

A sudden onset of illness was a usual feature in these cases. Two of these were proved to be due to psittacosis-ornithosis infection, and 22 had cold-agglutinin-positive tests and are tentatively grouped together as "primary atypical pneumonia, aetiology unknown." None of these cases had antibodies to influenza viruses A and B, but this group may still prove to be a mixed one. They showed no tendency to occur in epidemics, but were sporadic throughout the whole year. Some of them had a marked tendency to haemolytic anaemia, though this may also occur in other viral pneumonias.

No cases of Q fever were found throughout the investigation.

I am greatly indebted to Dr. B. P. Marmion, Dr. A. D. Macrae, and Dr. A. P. Goffe, of the Group Laboratory, Colindale, for the virus investigation of the cases described. I am also grateful to

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ROLE OF STATISTICS IN REGIONAL HOSPITAL PLANNING

WITH SPECIAL REFERENCE TO THE BIRMINGHAM HOSPITAL REGION

BY

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Before the inception of the National Health Service on July 5, 1948, there was no unification of the organization of the hospital services in this country. The main types of hospitals were those supported by voluntary contributions and those maintained by local authorities. Within any one area the development of each type was independent of that of another except so far as both were reliant upon contributions extracted either voluntarily or compulsorily from the residents of the area in which they were situated. The inauguration of the National Health Service led to new methods of financing the hospital service—namely, the collection of funds (in the form of National Health stamps and taxation) by the State from a large proportion of the population. It is now possible, therefore, to plan an overall health service without reference to regional differences in the distribution of the nation's wealth.

Many estimates of the desired ratio of beds to population have been given both by Government-sponsored committees and by independent workers, as cited in Table I, which shows considerable variation with respect to a putatively adequate bed/population ratio. All these estimates are much higher than any actual ratios referable to the Birmingham Region, overall figures for which are included in the same table.

The region encompasses five counties—Herefordshire, Shropshire, Staffordshire, Warwickshire, and Worcestershire. Its total population on December 31, 1947, was

TABLE I.—*Estimates of Number of Hospital Beds Required for Each 1,000 Persons*

Estimate	Type of Bed				
	General	Chronic Sick	Isolation	Tuber-culosis	Maternity
Surrey plan	6·0		0·75	1·0	
Berks, Bucks, and Oxon scheme	5·5	2·5	0·60	0·7	
Scottish survey ..	4–8	1·5	1·50	1·7[1]	0·96[3]
Consultant services (M.O.H.)	Approx. 6·5	1·5	0·60	Not shown	1·00[4]
Hospital survey U.S.A.	4·5–5·5	2·0	Not shown	1·7[2]	
Birmingham Region:					
Total bed complement	2·85	1·44	0·47	0·52	0·39
Available complement	2·53	1·34	0·24	0·24	0·38

Approximate requirements in Birmingham Region based on: [1] 2 beds per death per annum. [2] 2·5 beds per death per annum. [3] 4–5 beds per 100 births. [4] Including antenatal beds.

4,259,500, of which some 60% are resident in the Birmingham–Wolverhampton conurbation, while Herefordshire and Shropshire are rural counties with a low density of population. The distribution of hospital beds within the region varies considerably from district to district, but not necessarily in accordance with their needs (Table II). In one rural area the overall ratio of

TABLE II.—*Numbers of Beds per 1,000 Persons in Various Areas in Birmingham Region (June 30, 1949)*

Bed	Rural Area		Suburban and Dense Rural Area		Dense Urban Area			
					1		2	
	Total	Avail-able	Total	Avail-able	Total	Avail-able	Total	Avail-able
General ..	3·66	3·46	2·65	2·57	3·36	2·49	2·76	2·62
Chronic sick ..	1·90	1·60	2·26	1·87	0·34	0·32	1·26	1·20
Fever	0·66	0·28	0·87	0·44	0·58	0·14	0·52	0·28
Tuberculosis ..	0·70	0·70	0·55	0·55	0·22	0·17	0·59	0·57
Maternity ..	0·53	0·53	0·46	0·46	0·42	0·38	0·42	0·42
Total ..	7·45	6·57	6·79	5·89	4·92	3·50	5·55	5·09

beds (excluding mental) to population is 6.64 per 1,000, while in an area of high population density the ratio is as low as 3.35.

As yet most of the estimates of the requisite bed ratios are but inspired guesses, and until further information is available about the work done in hospitals it is not possible to provide more reliable figures. At present our problem is to remedy gross deficiencies in the hospital service; and a reasonable target for the immediate future is the provision of sufficient beds, so that the bed/population ratio of every locality is at least equal to the present average for the country as a whole. This done, it would be time enough to estimate future requirements on the basis of predicted changes in the age structure of the population (Enid Charles, 1935, 1948).

It is here pertinent to recall the words of Florence Nightingale, herself one of the early advocates for hospital statistics. Writing in 1860, she remarks: "I am fain to sum up with an urgent appeal for adopting this or some *uniform* system of publishing the statistical records of hospitals. . . . I have applied everywhere for information, but in scarcely an instance have I been able to obtain hospital records fit for any purpose of comparison." It is chastening to realize that she would find little improvement if she were alive to-day. It should be recognized that regional authorities have far too little available information as a basis for day-to-day administrative decisions. A single example brings this deficiency into focus. There is at present a serious shortage of

hospital nurses, and in the Birmingham Region alone some 8% of hospital beds are closed because of insufficient nursing staff. It is not therefore profitable to lay down plans for large new hospitals without concomitantly making plans for a reorganization of the nursing services by more economical use of trained staff, perhaps also by a change in the present system of nurse recruitment and nurse-training. Table III shows differences in nurse/bed ratios (midwives are excluded) in the various types of hospitals. Recently more precise information with regard to work done by them has made possible a more detailed classification (Table IV).

TABLE III.—*Types of Hospitals and Nurse/Bed Ratios*

Type	Definition	No. of Nursing Staff* per 100 Beds
1. Chronic sick	Chronic sick only with the exception of a small proportion (less than 5%) for maternity, V D , or skin diseases	23·1
2. Convalescent	Recovery and rehabilitation	17·2
3. Cottage ..	Small general hospitals with fewer than 50 beds	41·0
4. Isolation ..	Infectious diseases (excluding tuberculosis) only	28·5
5. General ..	Primarily general medical, surgical, gynaecological cases and children. No specific allocation for chronic sick cases	47·8
6. General and chronic sick	General hospitals as (5) but with a specific allocation of beds for chronic sick cases	31·3
7. Maternity ..	Obstetrical cases, including in some cases immature baby units	14·7
8. Mental ..		13·3
9. Mental deficiency	Defined by statute	13·2
10. Special ..	Hospitals restricting their services to special types of patients—e.g., orthopaedics, E.N.T., etc., excluding tuberculosis (see 11 and 12)	42·1
11. Tuberculosis	Sanatoria admitting tuberculosis patients only	20·4
12. Tuberculosis and fever	Hospitals catering for patients suffering from tuberculosis and other infectious diseases	33·6

* Excluding midwives.

TABLE IV

1. General (large).—General hospitals of 100 or more beds having at least 10,000 new out-patients annually.
2. General (medium).—General hospitals of 100 or more beds having less than 10,000 new out-patients annually.
3. General (small).—Hospitals of less than 100 beds (including cottage hospitals)
4. General and Chronic.—Mainly (at least 50%) general, but also having a specific allocation of beds for chronic sick cases.
5. Chronic and General.—Mainly (at least 50%) chronic sick, but also having a specific allocation of beds for general cases.
6. Chronic.—Chronic sick hospitals, except for a small proportion (about 5%) of beds for other types of patients.
7. Convalescent —As in Table III.
8. Maternity —Ditto.
9. Mental —Ditto.
10. Mental Deficiency.—Ditto.
11. Isolation —Ditto.
12. Tuberculosis.—Ditto.
13. Tuberculosis and Isolation.—Ditto.
14. Orthopaedic Hospitals.—Non-acute orthopaedic surgery including short-term and long-term cases.
15. Specialist Hospitals.—As in Table III.

Role of a Regional Statistical Department

The example last cited emphasizes the need for factual knowledge of existing facilities as a basis for planning the future of the hospital service. To accumulate, assimilate, and interpret such knowledge a statistical department is essential, its role being to provide information for (*a*) assessing the current situation; (*b*) estimating future requirements; and (*c*) costing of hospital services.

Illustrations of methods used to ascertain the present situation in the Birmingham Region will call for comment at a later stage. It must be stressed in this connexion that considerations of time, money, and labour have sometimes provoked an empirical approach. The assessment of future requirements depends on knowledge of future trends in population and present-day demands on hospital beds. Enough work has been published on the former to justify confidence in short-range predictions about future populations. Large-scale surveys of hospital practice, such as have been undertaken by the Nuffield Provincial Hospitals Trust (1948), the General Register Office (MacKay, 1951), and the work at present being undertaken by the Department of Medical Statistics, University of Birmingham, in conjunction with the Birmingham Regional Hospital Board, regarding admissions to hospitals in the Birmingham Region, should provide useful relevant information with respect to present-day demands.

The necessity for economy in Government expenditure has recently focused attention on various methods by which the cost of hospitals can be assessed on a comparative basis. A review of financial costing methods lies outside the scope of this paper, but it is relevant to consider here the units by which hospitals will be compared, as they are based on statistical data collected from individual hospitals. A prerequisite of comparative statistics is that like should be compared with like. This, some might say, precludes comparative hospital statistics, for they regard each hospital as unique. However, there are others who believe that some form of comparative costing is inevitable if efficient use is to be made of the restricted budget now available for the hospital service. Since at the present time the second point of view is operationally more useful it is as well to consider here the fallacies which may be encountered.

To assess work done for in-patients a unit such as one bed-day may be used. It is clear that the cost of keeping a bed occupied for one day in a hospital for the chronic sick is certainly less than that in a general hospital; but differences of this type can be minimized if care is taken to restrict comparisons to hospitals of the same type (see Table IV). The difficulties in comparative costing arise in those hospitals with an out-patient department and which employ services such as pathological laboratories, *x*-ray departments, physiotherapy, and so on. A varying proportion (in some cases it is very high) of the hospital budget is expended on these services. At present no satisfactory definitions of units of work in these various departments are available. For example, one attendance at out-patients is equivalent, for costing purposes, to one treatment in the physiotherapy department or to one pathological specimen. (Ministry of Health circular R.H.B. (51) 59, H.M.C. (51) 56, B.G. (51) 57 says: "A single specimen of blood, urine, cerebrospinal fluid, etc., should be counted as one, however many investigations are performed.") Thus a specimen of urine for microscopical examinations counts as equivalent to a 5-ml. specimen of blood which might be used for several haematological and biochemical tests. Moreover, the practice varies from laboratory to laboratory: in one it may be preferred to collect one large sample of blood for several tests and in another to collect separate specimens for different tests. Although 20 pregnant women may attend one gymnastic class supervised by one physiotherapist, for costing purposes *each* counts as a treatment and is thus equivalent to the examination of a specimen of blood involving several tests for which the services of a pathologist, biochemist, and one or more technicians may be required.

Co-operative participation in collecting hospital statistics cannot be expected when the deficiencies in definition

are so apparent. Statistical departments can play an important and useful part in the planning and efficient management of the hospital service ; but their credentials will fall into disrepute if they fail to advise caution in interpreting figures and translating them into administrative action without sufficient recognition of their limitations.

Survey of the Facilities for Treatment of Malignant Disease in the Birmingham Region

A survey was undertaken to assess the adequacy of existing facilities for the treatment of malignant disease, with particular reference to the provision of beds for radiotherapy. For this purpose a census of all patients in hospital on one day was taken. They were classified as : (*a*) suffering from malignant disease, in hospital for investigation on its account, and in hospital for non-malignant conditions ; (*b*) occupying beds allocated to radiotherapy, beds specially reserved for malignant disease, and beds in general surgical, medical, or other wards. Tables V and VI show some of the results.

TABLE V.—*Patients in Hospital on Account of Malignant Disease, November 1, 1950.*

Patients Admitted for	No.	%
Radiotherapy	109	12
Radiotherapy combined with other treatment	53	6
Special medical or surgical treatment only	265	29
Nursing care (no special treatment)	251	28
Investigation	220	25
Total number	898	100

TABLE VI.—*Treatment of Malignant Disease by Type of Hospital.*

Type of Hospital	Total No. of Patients Admitted for Malignant Disease	Percentage of Patients Undergoing Various Treatments				Percentage of Patients Admitted for Investigation
		Rad. Ther. Alone	Combined R.T. and Other	Other	None	
A	340	28·8	7·4	35·3	3·5	25·0
1	56	—	—	45·0	23·0	32·0
2	124	2·4	7·2	30·0	22·5	37·0
3	28	—	—	35·5	39·5	25·0
4	168	1·0	9·0	30·0	37·0	23·0
5	40	—	—	—	72·0	28·0
6	106	2·0	2·0	8·5	79·0	8·5
7	2	—	100·0	—	—	—
9	22	13·5	—	36·5	45·5	4·5
14	1	—	—	100·0	—	—
15	11	9·0	—	36·5	18·0	36·5
Total	898	12·0	6·0	29·5	28·0	24·5

Note.—The types used in this table are the same as those shown in Table IV except that general hospitals of type 1 with a specific allocation of beds for radiotherapy have been classified separately as type A.

Of the confirmed cases, 38% were receiving surgical or medical treatment only, 36% were receiving no special treatment, 18% receiving radiotherapy only, and 8% were being treated by a combination of radiotherapy and surgical or medical measures. On the day of the census there were 172 patients receiving treatment involving radiotherapy. If we assume this number to be the daily average of beds occupied by such patients, the total number of beds required to be allocated to radiotherapy would be about 175.

In view of the fact that 28% of all patients in hospital on account of malignant disease were receiving no special treatment, their cases being presumably too far advanced for effective measures, it might be desirable to check the methods of cancer registration to ensure that such cases are included. Such cases are often seen initially in surgical out-patient departments and are later admitted to hospital (particularly those of types 5 and 6) for nursing care in the terminal stages.

The census method used in this survey is a speedy and economical way of obtaining an overall picture of the hospital services in the region. But as it is a sample of the hospital population on one day only it may be attended with considerable error. This can be reduced somewhat by suitable selection of the census day—holidays such as Christmas Day, bank holidays, and so on must obviously be avoided. If necessary the census can be repeated in different seasons of the year. In this region it is used as a stop-gap method until the results of the hospital discharge study discussed below are available.

Hospital Discharge Study

Many hospitals in this region are co-operating in a regional hospital discharge study. For this, a small form suitable for punch-card analysis is completed for every patient discharged from hospital. Information relating to age, sex, place of residence, duration of stay in hospital, and diagnosis is collected by this means. The analysis of these cards will provide data for estimating the requisite allocation of beds on the basis of present-day needs. The relative age incidence of diseases necessitating hospital admission is of interest in the prediction of future requirements, which must conform to the needs of a population changing with respect to its age structure. The average duration of stay is of value in determining whether the existing allocation of beds among the specialties is satisfactory.

It should be recognized that differences found between hospitals do not necessarily indicate that one is more or is less efficient than the other. The diversity of work undertaken, special local conditions, and many other factors operate to produce numerical differences, which can, however, be used to point out the need for further investigation.

Estimation of Hospital Catchment Areas

Most general and some special types of hospital commonly serve an area, more or less constant in size but difficult to delimit. We may conveniently speak of such an area as the catchment area of the hospital. Prior to the appointed day municipally administered hospitals had catchment areas clearly defined by the boundaries of the local authority ; and in most cases a residential qualification was necessary for admission ; but this was not true of voluntary hospitals, which admitted patients irrespective of their home address.

The National Health Service does not recognize any residential qualifications for admission to hospital. Theoretically, a patient may be admitted to any hospital in the country, but in practice patients find it convenient to be admitted to the nearest hospital offering facilities appropriate to their need. Moreover, general practitioners in a district know the staff of their local hospitals and they, too, commonly refer their patients to these.

In determining the population served by a particular hospital the first requisite is a knowledge of the admissions to hospital by their place of residence. At the time when the population survey was made the discharge slips mentioned above were not in use and consequently recourse was had to a census method as a temporary expedient. This entailed the following assumptions :

(1) That the hospital population on the census day gives a representative sample of that on any other day in the year.

Needless to say, this assumption is not legitimate if a substantial proportion of beds are available for treatment of conditions subject to considerable seasonal variation.

(2) That within each local administrative area the density of population is uniform throughout. In urban areas no great errors are likely to arise from this assumption, while in rural areas the number of persons involved is so small that even if there are considerable variations—for example, concentration of population in small towns and villages—the error will not be large.

On October 19, 1949, a census was taken of all patients in every hospital in the Birmingham Region. Each hospital completed a form showing the number of patients by the administrative area of their home; the information was transferred to punch-cards. Special hospitals, including mental and mental deficiency hospitals, were considered separately.

There were 107 local government areas in the region for which official estimates of population were available. The cards were sorted out according to these areas. Thus for each area the number of residents in hospitals on that day was known, and also the names of hospitals to which they were admitted. In most areas these numbers give a good estimate of the total hospital population on that day. Estimates for areas at the boundaries would not be so accurate, as no information was available regarding persons resident in these areas but in hospitals outside the region.

The method of determining the catchment areas from these data is shown in Appendix A.

Nursing Staff Requirements

Valid comparison of staff/bed allocation in different hospital groups must take stock of the fact that the target varies from hospital to hospital, the mean allocation presumably deemed adequate for mental hospitals in particular being far below the general. In the Birmingham Region the composition of the groups with respect to different types of hospitals is highly variable, and therefore a low staff/bed ratio for a particular management group does not necessarily signify that it is understaffed. Crude rates such as the number of nurses per 100 beds may therefore be very misleading, and it is necessary to interpret them in juxtaposition to some yardsticks of adequacy. Differences in the staff situation in hospitals of diverse types are exemplified in Table III. The overall nurse/bed ratio for any particular type of hospital is the number of nurses per 100 available—that is, open and ready for use—beds.

The problem would be simple if we had firm figures for the requirements of each type of hospital. In the absence of such figures, the calibration of any yardstick of adequacy we adopt must rely on arbitrary assumption; and it is not unreasonable to suppose that the overall figures in the region as a whole for any particular type of hospital listed in Table III are not far short of requirements. In any case, it is instructive to present the relevant information in such a way as to answer the question: "Does the staffing of the hospital exceed or fall short of the overall standard for the region as a whole?" The crude rate as defined above does not answer this question, but we can make an answer explicit by recourse to a Regional Standard Index (R.S.I.) which has the value 100 if the staff situation in the group is equivalent to that in the region as a whole. A value greater than 100 signifies that the current staff allocation is above, and a value less than 100 that it is below, the regional standard so defined. The method of computation of the R.S.I. is shown in detail in Appendix B. It involves the application of a simple standardization procedure (similar to that for age standardization in vital statistics) to the nurse/bed ratios of different hospital groups.

Summary

The role of statistics in the National Health Service is discussed.

Variations in the hospital needs of different localities are discussed and some estimates of the number of beds required for each 1,000 persons are shown.

The administrative uses of statistics are illustrated by reference to a survey on the hospital treatment of patients with malignant disease.

Future developments in the statistical service of the Birmingham Regional Hospital Board are outlined.

A method of obtaining the population of hospital catchment areas is given.

The use of standardization in administrative statistics is discussed, and an example is given of its use in making comparisons of staff/bed ratios between hospital management groups.

While it is a pleasure to acknowledge the assistance given to me in this work by the Birmingham Regional Hospital Board and its officers, it is necessary to point out that the views expressed are personal and should not therefore be attributed to that Board or any members thereof. I gladly acknowledge the guidance and encouragement which I have received at all times from Professor Lancelot Hogben, F.R.S., without which none of this work could have been done.

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APPENDIX A

Determination of Population of Hospital Catchment Areas

Let the total number of residents of area A who were in hospital on the census day be a; the number in B be b, etc. The total number of patients in regional hospitals on that day was $(a + b + \ldots + r + \ldots + x)$.

In Hospital *1* there were a_1 patients from A, b_1 patients from B, r_1 patients from R, etc.

In Hospital *2* there were similarly a_2, $b_2 \ldots r_2$, etc., patients from A, B, etc.

The proportion of in-patients from area A in Hospital *1* is

$$\frac{a_1}{a_1 + a_2 + \ldots a_x} = \frac{a_1}{a}$$

In most instances where area A is close to Hospital *1*, a_1 is very nearly equal to a.

Let the total population of A be n_a, of B be n_b, etc. Then the population of A served by Hospital *1* is:

$\frac{a_1}{a} \cdot n_a$, by Hospital *2* is $\frac{a_2}{a} \cdot n_a$, etc., and

$$n_a = a_1 \cdot n_a \div a + a_2 \cdot n_a \div a + \ldots + a_r \cdot n_a \div a + \ldots a_x \cdot n_a \div a$$

$$= \frac{n_a}{a}\left[a_1 + a_2 + \ldots a_r + \ldots a_x\right]$$

$$= \frac{n_a}{a}\sum_{r=1}^{r=x} a_r$$

The population of B served by Hospital *1* is $b_1 \cdot n_b \div b$ and of C is $c_1 \cdot n_c \div c$, etc.

Therefore the total population served by Hospital *l* is

$$a_1 . n_a \div a + b_1 . n_b \div b + \ldots + r_1 . n_r \div r + \ldots + x_1 . n_x \div x$$

The splitting-up of the population of an area is arbitrary, and where two or more hospitals are in juxtaposition it is more satisfactory to determine the catchment area for the group rather than the individual hospitals.

The estimates would be more satisfactory if they were based on hospital admissions over a period of time—say six months or a year. In this region, when the discharge slips are received from all hospitals further estimates of the catchment areas will be made on that basis. However, the census method is recommended as a speedy and economical technique when facilities are not available for a more detailed survey.

APPENDIX B

Calculation of Regional Standard Index

The rationale of the R.S.I. is as follows. The overall nurse/bed ratio in the region for any particular type of hospital listed in Table III is obtained thus: if R_n is the total number of nurses employed and R_b the total number of available—that is, beds open and ready for use—beds in any one type, then the overall staff/bed ratio in the region for that type of hospital is $100\ R_n \div R_b$. The overall ratios for June 30, 1949, are shown in Table III.

For each type of hospital in Table III we have the overall nurse/bed ratio, which may be denoted thus: $n_1, n_2 \ldots n_{12}$. For any particular management group our returns cite $b_1, b_2 \ldots b_{12}$ beds in one or other type of hospital, and $N_1, N_2 \ldots N_{12}$ nurses. If the staff situation tallies with that of the region there would be $n_x . b_x \div 100$ nurses in the *x*th type of hospital, and the total (standard) number of nurses would be:

$$N_s = \frac{1}{100}(n_1b_1 + n_2b_2 + n_3b_3 + \ldots + n_{12}b_{12})$$

Actually it is

$$N_t = N_1 + N_2 + N_3 + \ldots + N_{12}$$

If N_t exceeds N_s the hospital allocation is above par, and if N_t falls short of N_s it is below par. We may use $N_t \div N_s$ expressed as a percentage to convey this information. Thus we define the Regional Standard Index as:

$$\text{R.S.I.} = 100\ N_t \div N_s$$

Computation of Regional Standard Index

In the Tables below two part-time nurses are counted as equivalent to one full-time nurse.

Type of Hospital	Overall Ratio for that Type ($100\ n_x$)	No. of Available Beds	Estimated No. of Nurses Required $n_x . b_x \div 100$	Actual No. of Nurses Employed N_x
Hospital Management Committee A				
5. General ..	47·8	235	112	119·5
12. Tuberculosis and fever ..	33·6	59	20	25·5
7. Maternity ..	14·7	22	3	7·0
3. Cottage ..	41·0	9	4	4·0
3. Cottage ..	41·0	10	4	3·5
8. Mental ..	13·3	1,183	157	189·5
1. Chronic sick ..	23·1	290	67	48·5
Total ..		$B_t = 1{,}808$	$N_s = 367$	$N_t = 397{\cdot}5$
Hospital Management Committee B				
5. General ..	47·8	159	77	80·0
5. General ..	47·8	287	136	120·0
1. Chronic sick ..	23·1	176	41	40·5
7. Maternity ..	14·7	14	2	5·0
11. Tuberculosis ..	20·4	19	4	10·0
4. Isolation ..	28·5	12	3	2·0
11. Tuberculosis	20·4	22	4	4·5
Total ..		$B_t = 689$	$N_s = 267$	$N_t = 262{\cdot}0$

Crude rates $= 100\ N_t \div B_t$

Regional Standard Index $= 100\ N_t \div N_s$

	H.M.C. (A)	H.M.C. (B)
Crude rate ..	$\frac{100 \times 397{\cdot}5}{1{,}808} = 22$	$\frac{100 \times 262}{689} = 38{\cdot}8$
R.S.I.	$\frac{100 \times 397{\cdot}5}{367} = 108$	$\frac{100 \times 262}{267} = 98$

Thus from the crude rates it would appear that B has almost twice as many nurses as A, but when due allowance is taken for the differences in composition of the groups A is somewhat higher and B lower than the regional average.

PRIMARY TUBERCULOUS PLEURAL EFFUSION IN OLDER AGE GROUPS

BY

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The primary serous pleural effusion in children and young adults no longer presents an aetiological problem. Many series of cases, carefully investigated and laboriously followed up, have been reported in the literature, leaving no doubt that, with few exceptions, the tubercle bacillus, although seldom declaring its presence in the fluid, is lurking in the background, prepared in later years to exact a further toll on the health of the victim.

A similar effusion in adults over 40 years of age presents a much greater problem in diagnosis, because of the lessening incidence of tuberculosis and the increasing incidence of malignant disease. From the statistical point of view it is clear that, unless care is taken at the outset to exclude malignant cases from consideration, morbidity and mortality occurring during a follow-up period, especially if the investigator is dependent on a postal questionary without necropsy control, may be wrongly attributed to tuberculosis. It is of interest in this connexion that Fauvet (1945), as a result of a follow-up of 731 cases of serous pleural effusion, believes that tuberculosis morbidity and mortality increase with advancing years. On the other hand, Maclean (1948) fears that such a deduction may be erroneous, and that it is almost certainly due to the inclusion of a number of cases in which malignant disease is the real cause. The *British Medical Journal* (1946) points out that the prognosis with respect to the development of tuberculosis is much better in children than in young adults, but does not venture an opinion on adults over 40, in whom it states that "carcinoma of the lung is common."

Another statistical error may occur in all age groups, but more so in the older groups, if cases with the adult type of pulmonary tuberculosis complicated by effusion are included. As Thompson (1947) has pointed out, the prognosis in this type of case is that of pulmonary tuberculosis in general, and is therefore much worse than that of effusion occurring in the period after a primary infection. Radiology may fail to reveal an adult type of lesion until considerable absorption of the effusion has taken place; such a case may be wrongly included as a primary effusion.

The present investigation was undertaken to determine the frequency and prognosis of primary tuberculous pleural effusion in patients over 40. Case material was selected from admissions to five medical charges in the Royal Infirmary of Edinburgh during a period of five years, from 1945 to 1949. All patients aged over 40 found on admission to have a serous pleural effusion of uncertain aetiology were included initially in the investigation, and total 60 in number. Cases in which the pleural effusion was secondary to some obvious lesion in the lungs, heart, or elsewhere were excluded (except those in which the lung lesion was suggestive of the adult form of pulmonary tuberculosis). Two of the 60 patients selected left hospital against advice before investigations could be completed, and were therefore omitted from the final analysis. The remaining 58 were carefully investigated, and the follow-up is complete. Table I shows the ultimate diagnosis in these cases.

TABLE I.—*Ultimate Diagnosis in 58 Cases of Pleural Effusion of Uncertain Aetiology occurring in Adults over 40.*

Diagnosis	No. of Cases
Bronchial carcinoma	11
Tumours other than bronchial carcinoma	8
Simple inflammatory	7
Collagen disease	4
Cardiac transudate	2
Reticulosis	2
Pulmonary infarction	1
Adult pulmonary tuberculosis	2
Uncertain	1
Primary tuberculosis	20
Total	58

Comments on Diagnosis

Bronchial Carcinoma

Of the 11 cases, 1 was confirmed by necropsy, 2 by bronchoscopic biopsy, 1 by thoracoscopic biopsy, and 2 by the later development of unequivocal radiological signs; the remaining 5 were less certainly confirmed by the development of probable radiological signs and/or a rapid downhill clinical course with recurrence of massive blood-stained effusion and a fatal termination.

Tumours Other than Bronchial Carcinoma

Of the 8 cases, 4 were confirmed by necropsy, 1 by the development of undoubted (radiological) secondaries in the lungs, and 3 by the finding of malignant cells in the fluid associated with clinical or radiological evidence of a primary tumour elsewhere in the body.

Simple Inflammatory Cases

All 7 cases had been treated with a sulphonamide and/or penicillin before admission and had clear sterile effusions without definite radiological evidence of lung consolidation; 5 were regarded initially as possible tuberculous effusions, 1 as a possible malignant effusion (Case 6), and 1 as a possible simple inflammatory effusion (Case 7). Four cases had a predominance of polymorph neutrophils in the exudate, 1 a predominance of polymorph eosinophils, and 2 a predominance of ordinary lymphocytes. The subsequent course of events in each case was as follows:

Case 1.—Initial pyrexia subsided with further sulphonamide and penicillin, but subsequently became hectic, with leucocytosis; eventual cure occurred with the coughing up of a large quantity of pus, suggestive of pulmonary or pleuro-pulmonary abscess.

Case 2.—Pyrexia and fluid persisted. After discharge to a convalescent home the patient developed purulent sputum (negative for tubercle bacilli) and finger clubbing; subsequent investigation revealed a bronchiectatic lower lobe on the side of the effusion. The lobe was resected at thoracotomy, which revealed no evidence of tumour or tuberculosis; the original effusion was lymphocytic.

Case 3.—Pyrexia persisted and originally clear effusion became turbid; subsequent resection of empyema space showed no pathological evidence of tuberculosis.

Case 4.—Pyrexia subsided rapidly with further sulphonamide and penicillin. While convalescent the patient had a brisk haemoptysis. A radiological follow-up for four years showed gradual development of bilateral bronchiectatic changes.

Case 5.—Pyrexia had subsided before admission. Effusion contained 50% eosinophils. The Mantoux test (1:100) was negative, and has remained so during repeated tests over two years.

Case 6.—Pyrexia responded to further penicillin and sulphonamide; a subsequent relapse also responded. First aspiration—lymphocytes; second aspiration—lymphocytes plus possible malignant cells. The diagnosis of malignant disease was strengthened by the finding of a mass attached to the liver, but the patient was alive and well two years later. The mass is now thought to be an abnormal lobe of the liver. The condition is regarded as a simple inflammatory one because of the undoubted response on two occasions to sulphonamide and penicillin.

Case 7.—In addition to pyrexia and left pleural effusion, the patient had hypertension and auricular fibrillation, but there was no evidence of either left- or right-sided cardiac failure. The effusion was clear and sterile, but with polymorph exudate. Pyrexia responded slowly to penicillin and sulphonamide; the effusion cleared up, but localized coarse crepitations appeared and persisted in the left lower lobe, indicating resolving consolidation (not visible on *x*-ray film). The patient died of congestive cardiac failure some months after discharge.

Collagen Disease

Of the 4 cases, 1 presented with a bilateral pleurisy which went on to bilateral effusion with high temperature. The provisional diagnosis was miliary tuberculosis, but necropsy showed unequivocal evidence of disseminated lupus erythematosus. The remaining 3 cases presented with vague muscular pains, including chest pain, which was at first thought to be muscular in origin; all, however, developed bilateral effusion associated with a long-continued toxic illness, and eventually showed changes in the hands diagnostic of rheumatoid arthritis; 1 of the 3 cases had a predominance of eosinophils in the pleural fluid. Although it is impossible to exclude tuberculosis in those cases, it is regarded as important that in each case the fluid was bilateral and was associated with subsequent undoubted evidence of a disease known to involve diffusely all the fibrous tissues in the body. Bilateral effusion in tuberculosis is uncommon. Necropsy studies of cases of rheumatoid arthritis have shown that pleural fibrosis without evidence of tuberculosis, either past or present, is a common finding (Rosenberg, Baggenstoss, and Hench, 1944; Fingerman and Andrus, 1943).

Cardiac Transudate

Of the 2 cases, 1 presented with slight dyspnoea and was found to have a left-sided pleural effusion. Neoplasm and tuberculosis were being considered, when the patient died suddenly. At necropsy an unsuspected cardiac infarct, approximately three weeks old, was seen to involve the left ventricle. There was no evidence of neoplasm, tuberculosis, or lung infarct. The right pleural cavity was completely obliterated by old adhesions, thus accounting for the strictly unilateral nature of the

transudate. The other case has been reported previously (Robertson, 1951); this patient presented with a puzzling interlobar effusion which eventually proved to be cardiac in origin.

Reticulosis

One case presented with a right pleural effusion which was thought to be tuberculous in origin. Some months later signs of superior mediastinal obstruction and generalized lymphadenopathy developed: a gland biopsy showed a lymphoid follicular reticulosis, in which serous effusion is a common finding (Hadfield and Garrod, 1947). The other case was known to have a reticulosis of obscure type, gland biopsy suggesting the possibility of atypical Hodgkin's disease. Bilateral pleural effusion developed in the absence of radiological evidence of thoracic gland involvement. In view of the possible confusion pathologically between Hodgkin's disease and tuberculosis, the latter was considered in diagnosis. The effusions, however, proved to have a low protein content; this led to estimation of the plasma proteins, when the albumin was found to be 2.29 g.%. A high protein diet corrected the low plasma albumin, and the pleural fluid disappeared. It seems reasonable to conclude that the pleural effusions were transudates due to hypoproteinaemia complicating a reticulosis.

Pulmonary Infarction

This patient was in a hospital ward for investigation of gall-bladder disease. While in bed she developed an acute pleurisy, with subsequent rapid development of a clear serous effusion; there was no evidence of pneumonia. Haemoptysis appeared on the third day of illness. A pulmonary infarction seems the most probable diagnosis in view of the haemoptysis and the onset of illness while in bed; there was, however, no evidence of thrombophlebitis, and tuberculosis had been considered prior to the haemoptysis.

Adult Pulmonary Tuberculosis

Two cases had radiological changes in the lungs suggestive of this condition: in both, the sputum was found to contain tubercle bacilli. It should be noted that the number in this group is artificially small, as such cases are not admitted to the Royal Infirmary of Edinburgh if alternative accommodation can be obtained.

Uncertain

This patient, known to have hypertension, was resting in bed at home. She developed a febrile illness with pleuritic pain and copious purulent sputum, and a clear serous lymphocyte effusion subsequently occurred. All investigations for tuberculosis were negative. A follow-up for four years showed recurrent bronchitis, asthma, obesity, and hypertension. As the main illness took place at home and she was seen only when the effusion was clearing up, it is difficult to suggest a diagnosis: "simple inflammatory" seems a more probable diagnosis than tuberculosis.

Primary Tuberculosis

Of the original 58 cases 38 have been described above, leaving 20 in which a diagnosis of primary tuberculosis was made. It should not be thought, however, that this diagnosis rests entirely on a process of exclusion. Of these 20 cases 14 had an illness resembling in every respect the classical primary tuberculous effusion in the young adult—that is, sudden onset, in a previously healthy person, of acute pleuritic pain progressing to a clear serous lymphocytic effusion, with no radiological evidence of lung disease, and pursuing a protracted febrile course unresponsive to chemotherapy and antibiotics. Five others of the 20 had a similar illness, but the onset was more insidious, and there was little or no pleuritic pain. The remaining case had an acute pleurisy progressing to effusion, without pyrexia at any time. In only two cases was the tubercle bacillus isolated from the pleural fluid; this does not invalidate the diagnosis, since in similar cases in young adults it is notoriously difficult to isolate the bacillus unless special methods are used. No case had tubercle bacilli in the sputum or gastric washings. *X*-ray films of the chest after clearing of the effusion did not reveal any case of adult pulmonary tuberculosis. Follow-up has excluded any disease, other than tuberculosis, which might have accounted for a pleural effusion.

Discussion

In this series of 58 cases of serous pleural effusion of initially uncertain aetiology occurring in adults over 40 years of age, only 20 could be ascribed to primary tuberculous infection. Nineteen proved to be secondary to malignant disease of the lungs or elsewhere. Only two were due to the adult form of pulmonary tuberculosis, but this is an artificially small number because of the restricted admission of this type of case to a general hospital. Details of the remaining 17 cases have been included to justify their grouping under miscellaneous conditions given in Table I.

As stated earlier, this series of cases was selected from admissions to five medical charges during a period of five years from 1945 to 1949. In order to find the relative frequency of primary tuberculous effusion in adults over 40, the corresponding numbers of cases of primary tuberculous effusion in children and young adults admitted to the same five charges over the same period of time were determined. The details are given in Table II. It was found that almost 10% of primary tuberculous effusions occur in adults aged over 40.

TABLE II.—*Age Distribution of 216 Cases of Primary Tuberculous Pleural Effusion Occurring over a Five-year Period*

Age (Years)	No. of Cases		%	
Under 20	117		54·1	
20–29	60		27·8	
30–39	19		8·8	
40–49	12		5·5	
50–59	3	20	1·4	9·3
60–69	4		1·9	
70–79	1		0·5	
Total	216		100	

It is difficult to estimate how many people in Great Britain over 40 are tuberculin-negative. Recent tuberculin surveys have concerned children and young adults, but in 1934 Kayne found that among non-tuberculous admissions to a general hospital in London 15% of the 45–59 age group and 14% of the over-60 age group were tuberculin-negative. Those figures are probably artificially high, as it is well known that debility and intercurrent illness in hospital patients may inhibit the tuberculin reaction. In a recent paper from Norway, Jonsen and Ustvedt (1950), using a combination of Mantoux and B.C.G. tests, conclude that lack of tuberculous allergy in old people is not so common as has been assumed, being in the region of 12%.

While there may be some doubt about the precise number of older people liable to acquire a primary

infection, Terplan (1940) and Pagel (1948), in their pathological studies, have proved beyond question that primary infection does occur. Terplan in addition has shown that an older person may acquire a "second" primary infection when the "first" primary infection has become completely inactive (presumably with reversion to tuberculin negativity). Kayne, Pagel, and O'Shaugnessy (1948) believe, further, that an old primary infection may commonly flare up in people over 45 years. It would seem, therefore, that a primary tuberculous effusion may occur in older people following delayed primary infection, reactivation of old primary infection, or "second" primary infection.

In the present series of 20 cases, one case which came to necropsy showed reactivation of a primary Ghon focus. Most of the 20 had lived in large cities since early childhood and therefore had every opportunity of acquiring infection earlier in life. No case had a history of recent contact with a known source of infection. Only one case showed radiological evidence of hilar gland enlargement, this being the only point in which the clinical picture differed from that of similar effusions in children and young adults, in whom such radiological evidence is much more common. This difference has been noted previously (Landau, 1949), and may mean that in the older person a typical primary complex, in which hilar gland enlargement is usually marked, is not commonly present. It is not possible to draw definite conclusions from this series of cases, but it would seem that delayed primary infection, in its typical form, is probably not an aetiological factor.

While it has been proved (Graham, 1925; Smithers, 1934; Vaizey and Perry, 1940; Landau, 1949) that primary tuberculous effusion in children has a surprisingly good prognosis, there is little agreement in the literature concerning the influence of advancing years. Thompson (1946), whose series of 233 cases included only 13 over 40 years of age, considers that age *per se* does not matter with respect to the development of tuberculous lesions. On the other hand, Fauvet (1945), Gaarde (1930), and Farber (1943) show that in those over 40 years of age the prognosis tends to become worse. It is unfortunate that many series in the literature include no cases older than 40, and that those which do have, of necessity, all too few for statistical purposes. The old enemies, inadequate follow-up and doubtful diagnosis, also play a part in invalidating statistics.

Unfortunately, the present series of 20 cases over 40 years of age is also small, but efforts have been made to eliminate errors in diagnosis, and follow-up over a period of three to six years is complete. All surviving cases have been examined clinically and radiologically, and necropsy has been performed on those who died. Table III indicates that the incidence of tuberculous morbidity is 45%, with a corresponding mortality.

TABLE III.—*Follow-up of 20 Cases of Primary Tuberculous Pleural Effusion in "over 40" Age Group*

	No. of Cases
Alive and well	11
Dead—Pulmonary tuberculosis	2
" —miliary "	1
" —pericardial "	1
Alive—active pulmonary tuberculosis	3
" —inactive " "	1
" —recurrence of effusion on other side	1

Although no sweeping deductions can be made from this small series, it is clear that the primary tuberculous effusion is a potentially serious disease in older people. The morbidity figure of 45% compares unfavourably with the average morbidity of 14% calculated from nine series of cases of primary effusion, mostly in younger age groups, published beween 1945 and 1949. That its potential gravity is perhaps not fully appreciated is illustrated by the fact that only 9 of the 20 cases received a period of treatment at a convalescent home before being returned to normal life; and in only 3 was that period longer than one month (it so happens that those 3 are alive and well). It may be that the bad prognosis in this series is partly due to this factor. In comparison, virtually all children and young adults with effusion have a prolonged period of convalescence. It would seem that efforts should be made to secure adequate convalescence for all cases of effusion, irrespective of age.

Summary

An investigation is presented in which an attempt has been made to elucidate problems relating to the frequency and prognosis of primary tuberculous pleural effusion in the older age groups.

In a series of cases in adults over 40 years of age presenting with a serous pleural effusion, approximately one-third proved to have a primary tuberculous effusion; in the remainder the effusion proved to be secondary to some other condition.

Approximately 10% of all primary tuberculous pleural effusions occur in adults over 40.

The aetiology of primary tuberculous pleural effusion in older age groups is discussed in relation to delayed primary infection, reactivation of an old primary infection, and a "second" primary infection. No definite conclusion is reached, but delayed primary infection seems an unlikely aetiological factor.

Difficulties in assessing the prognosis of primary tuberculous pleural effusion in the older age groups are discussed. The present investigation suggests that subsequent tuberculous morbidity is greater in them than in children and young adults.

The early part of this investigation was carried out with the help of a grant from the Royal Victoria Hospital Tuberculosis Trust. I am greatly indebted to the physicians of the Royal Infirmary of Edinburgh who allowed me access to their cases and case records. I wish to thank Professor Charles Cameron for his kindly criticism.

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The use of blood has increased more than twofold since the beginning of 1946. Part of this increase may well be fully justified, but there is probably also avoidable waste. Continuous supervision of blood banks is essential: an average blood bank may be said to be running economically and efficiently if not more than 10 to 15% of the blood issued to it by the Regional Transfusion Centre is returned unused, and if this is fit for conversion to plasma. The Ministry of Health has issued suggestions on how this can be achieved.

RADIOLOGICAL CHANGES IN THE SKULL IN DYSTROPHIA MYOTONICA

BY

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In a previous endocrine study of dystrophia myotonica Caughey and Brown (1951) made reference to certain radiological abnormalities of the skull in dystrophia myotonica, and suggested that these changes should be regarded as variable features of the disorder. Since that time I have had the opportunity of studying further cases which have presented with similar radiological findings. No mention of these findings has been discovered in the standard textbooks, and this additional account is recorded in the hope that it may stimulate interest and establish the clinical significance of these changes by radiological study of many more cases than one observer can hope to collect.

Historical

Myotonia was first described by Leyden in 1874. In 1876 Thomsen, who himself suffered from myotonia, recorded his own symptoms and signs. The combination of myotonia and muscle atrophy was described by Dana in 1888, but it is Déléage (1890) who is usually credited with the first account of dystrophia myotonica. In 1909 Steinert wrote a full description of the disease, and first described changes in the mental state and some of the associated dystrophic features such as premature frontal baldness and gonadal atrophy. At the time, these latter findings were regarded as being merely coincidental. In 1911 Greenfield recorded the constant association of cataract in the disorder, and thereafter the other dystrophic manifestations of the disorder came to be recognized as an essential part of the clinical picture in the fully developed disorder of the "dystrophic" generation.

Few authors have made reference to radiological changes in the skull in these patients. Scharnke and Full (1920) described a large frontal sinus in the presence of a normal pituitary fossa. Rouquès (1931) reported the radiological findings of the skull in four patients. The calvarium was distinctly thickened in three and less so in the fourth. Large frontal sinuses occurred in two, in two the pituitary fossa was small, and in two it was bridged over by an area of calcification. Fagin (1946) reported the occurrence of hyperostosis frontalis in two patients.

Clinical Reports

This study is based on 13 patients with dystrophia myotonica—all members of the so-called "dystrophic generation" and all presenting myotonia, characteristic muscle-wasting, and various dystrophic lesions such as cataract, gonadal atrophy, and frontal baldness. It is considered that in none of these cases can there be any reasonable doubt about the diagnosis. Most of them have been reported in detail elsewhere, and are here recorded in brief but with full radiological reports.

Case 1.—A farmer aged 45, single, developed weakness and wasting of the arms and legs and myotonia at the age of 27. The weakness progressed until he became almost bedridden. Soon after the onset of the disease he developed bilateral cataract, premature frontal baldness, and gonadal atrophy. Post-mortem findings confirmed the diagnosis of dystrophia myotonica, with the disorder fully developed. *Radiological findings:*—Skull (Fig. 1): the vault shape was normal; the calvarium was thickened; hyperostosis interna frontalis et parietalis was present; the sinuses were within normal limits; the mandible was normal; the pituitary fossa was small, with a pneumatized dorsum sella; the pineal body was calcified.

Case 2.—A single panel-beater aged 26 presented with auricular flutter in 1945. Myotonia had been noted two years prior to this. He had the fully developed disease, with myotonia, wasting of the face, arms, legs, and sterno-mastoid muscles. There was no gonadal atrophy and no cataract. *Radiological findings:*—Skull: the vault shape was normal and the calvarium thickened, especially in the posterior parietal region; there was a hyperostosis interna frontalis; the frontal sinuses were deep; the sphenoidal sinus was large and the pituitary fossa very small.

Case 3.—A married woman aged 33 developed myotonia at 21. Wasting and weakness of legs, arms, face, and neck

FIG. 1.—Case 1. Calvarium thickened; hyperostosis frontalis; pituitary fossa small.

muscles were apparent at 28, and bilateral cataract developed at 30. *Radiological findings:*—Skull: the vault shape was normal and the calvarium thickened throughout, with moderate hyperostosis interna frontalis et parietalis; the sphenoidal sinus was large and other sinuses were within normal limits; there was pneumatization of the dorsum sella; the pituitary fossa was small, and the pineal body was calcified.

Case 4.—A male factory-hand aged 27 had for two years noted myotonia, weakness of the neck muscles, wasting of the forearms and legs, and frontal baldness. He presented with myotonia and characteristic muscle-wasting. There were no lenticular opacities, and no gonadal atrophy was noted. *Radiological findings:*—Skull: the calvarium was thickened and there was hyperostosis interna frontalis; the sinuses were normal in size; the pituitary fossa was small.

Case 5.—A military pensioner aged 32 first noted myotonia while a prisoner of war in Germany in 1942. In 1946 he presented with myotonia, wasting of sterno-mastoids, forearms, and legs. There was cataract and frontal baldness, but gonadal atrophy was not noted. *Radiological findings:*—Skull: the calvarium was normal; there was a very grossly calcified falx cerebri, which was responsible in part for the appearance of a nebula frontalis; no definite hyperostosis was present; the pituitary fossa was normal to small; all sinuses were large.

Case 6.—A carpenter aged 41 developed failure of potentia at 34. Myotonia was noticed four years later, and wasting

of face, neck, forearms, and legs became apparent. He presented a characteristic picture, with myotonia, muscle-wasting, and gonadal atrophy. *Radiological findings*:—Skull: there was no thickening of the calvarium; the frontal and sphenoidal sinuses were extensive and deep; the pituitary fossa was small; the dorsum sella was completely pneumatized; the jaw was prognathous.

Case 7.—A housewife aged 51 had noticed weakness of her neck muscles since she was 30. The sterno-mastoid muscles had wasted, there was progressive wasting and weakness of her forearms and legs, and she had bilateral cataract. Mechanical myotonia was present. The ankle-jerks were absent. *Radiological findings*:—Skull: there was thickening of the whole calvarium with loss of differentiation of the cortex and the diploe and extensive hyperostosis interna frontalis. The sinuses were normal and the pituitary fossa was very small, with calcification near the floor. There was no pneumatization of the dorsum sella.

Case 8.—A labourer aged 28, who had been backward at school, at 17 noticed difficulty in relaxing his grasp, and his arms and legs became progressively weaker and wasted. Visual deterioration had been apparent for five years. He presented with myotonia, muscle-wasting, bilateral lenticular opacities, and frontal baldness. The gonads were not obviously atrophic. *Radiological findings*:—Skull: the vault was normal in size and the calvarium was thickened; there was extensive hyperostosis interna frontalis et parietalis; the vertical component of the frontal sinus was normal, but the horizontal component extended almost to the anterior clinoids; the pituitary fossa was very small, and the dorsum sella was thick and partially pneumatized.

Case 9.—A grocer aged 33, who was backward at school, first noticed myotonia at 13 years. Wasting of face, arms, and legs developed two years later. He presented with marked myotonia, wasting of sterno-mastoid muscles, and face, forearms, and legs. There was marked gonadal atrophy, but there were no cataracts. *Radiological findings*:—Skull (Fig. 2): the vault was small, globoid, and microcephalic; the calvarium was thickened but of normal density; the sinuses were extensive and deep, especially the sphenoids, which extended into the posterior clinoid processes; the pituitary fossa was very small and the jaw markedly prognathous.

FIG. 2.—Case 9. Calvarium thickened; pituitary fossa very small; jaw prognathous; sinuses extensive.

Case 10.—A spinster aged 45 had been admitted to a mental hospital nine years previously. Six years later she developed myotonia, and in 1950 presented with bilateral cataract, myotonia, and wasting of the face, sterno-mastoid muscles, forearms, and legs. *Radiological findings*:—Skull: there was marked hyperostosis interna frontalis; the floor of the anterior fossa was more vertical than usual and the pituitary fossa was small; the frontal sinus showed a large horizontal component and a very large vertical component; the sphenoidal sinus was large and the antra were normal; the jaw was prognathous.

Case 11.—A housewife aged 47 developed bilateral cataract nine years previously. When examined she presented myotonia of grasp and some weakness of the sterno-mastoid muscles. *Radiological findings*:—Skull: the calvarium was thickened; there was hyperostosis interna frontalis; the pituitary fossa was small and the sinuses were all normal.

Case 12.—A farmer aged 42 first noticed myotonia in 1941, and weakness and wasting of his arms and legs developed a year later. He presented with myotonia and wasting of the sterno-mastoid muscles, forearms, and legs. There was bilateral cataract, with frontal baldness, gonadal atrophy, and areflexia. *Radiological findings*:—Skull: the calvarium was normal; there was no hyperostosis; the pituitary fossa was small; the frontal sinuses were extensive and the sphenoidal sinus was large.

Case 13.—A spinster aged 42 had for 15 years noticed an inability to relax her grasp. For 15 months her legs had been weak and wasting had developed. On examination there was wasting of the face, forearms, and legs, and the sterno-mastoid muscles had wasted completely. There was myotonia of grasp. *Radiological findings*:—Skull: there was marked thickening of the calvarium, the average thickening being approximately 1.5 cm. This thickness was evenly distributed and involved all the bones of the vault. There was also evidence of some hyperostosis interna frontalis. The pituitary fossa was also abnormally small. Both anterior and posterior clinoid processes and the dorsum sella were well developed.

Discussion

These 13 patients all suffered from dystrophia myotonica and all were members of the so-called "dystrophic generation." It is realized that in assessing the size of the pituitary fossa and the size of the sinuses in the standard views the radiologist bases his opinion largely on subjective impression, as strictly accurate measurement is not always possible.

In the above reports the size of the pituitary fossa is classified as normal, small, or very small—"small" indicating a sagittal diameter below 9 mm. and/or a vertical diameter below 6 mm.; "very small" indicating measurements below 6 mm. and/or 4 mm. respectively for the same diameters. With two exceptions the magnification distortion was known to be the same in all cases.

The pituitary fossa was small in seven cases, normal to small in one, and very small in five. Thickening of the calvarium occurred in nine cases. The next most constant finding was the presence of hyperostosis interna frontalis et parietalis, which was noted in nine and was pronounced in three of these. It is notable that five of these cases were males aged from 26 to 45 years. Enlargement of the sinuses was noted in eight, and in two the mandible was elongated.

In view of these findings it seems evident that these radiological abnormalities of the skull must come to be accepted as one of the variable dystrophic features of dystrophia myotonica.

Summary

Thirteen cases of dystrophia myotonica are reported in brief. All presented some radiological abnormalities of the skull. The most constant changes were a small to very small pituitary fossa, thickening of the calvarium, and hyperostosis interna. There was enlargement of the sinuses in some and in two the mandible was elongated. We believe the high incidence of these changes cannot be coincidental, and it is held they should now come to be accepted as some of the variable features of dystrophia myotonica.

It is a pleasure to thank various physicians who have given me access to their cases, and Dr. Alexander and Dr. Rolleston for reviewing the radiological reports.

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BULLOUS LESIONS IN LEUKAEMIA

BY

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The skin manifestations of leukaemia are many and varied : Arzt and Fuhs (1929) have mentioned eczematous, erythema-multiforme-like, purpuric, zosteriform, urticarial, bullous, and rupial lesions, in addition to exfoliative erythrodermia and the specific leukaemic deposits occurring in the form of small papules, nodules, or large tumours.

Wiener (1947) states that bullous eruptions may precede generalized exfoliative erythrodermia in lymphatic leukaemia, and that they are often encountered in the early stages of monocytic leukaemia. It would seem that remarkably few cases of leukaemia with bullous lesions have, in fact, been recorded. In an analysis of a series of 445 cases of the reticuloses (including 160 cases of leukaemia) at the Los Angeles County Hospital, Epstein and MacEachern (1937) reported cutaneous involvement in 194 (43.5%). Bullous or vesicular lesions were seen in six cases, of which three were Hodgkin's disease, two myeloid leukaemia, and one lymphosarcoma. No bullous eruption was seen in any cases of lymphatic, monocytic, or acute leukaemia.

Margarot, Rimbaud, and Roche (1935) reported the case of a boy of 12 years, who was first seen with a purulent bullous eruption on the lower limbs, associated with pyrexial attacks. It was only when, five months later, he developed a generalized erythrodermia associated with palpable lymph nodes that a blood count revealed a leucocytosis of 34,000 per c.mm., of which 91% were primitive cells of the lymphatic series. The diagnosis of acute leukaemia was confirmed by the subsequent course of the disease, with the development of ulcerative stomatitis and a severe bleeding tendency, and death within four months of establishment of the diagnosis.

Remenovsky (1935) described the case of a 51-year-old patient with an acute leukaemia (leucocytes 83,600 per c.mm., 91.7% immature lymphocytes). After systemic arsenic the blood picture changed dramatically, the total leucocyte count falling to 6,000 per c.mm., 40% being lymphocytes. At the same time bullous eruptions developed on the wrists and forearms.

It would seem that the few recorded cases of bullous dermatoses have been associated with acute leukaemia. The following case of chronic lymphatic leukaemia is therefore of particular interest because of several unusual features : the manner of presentation as a bullous eruption on the palms and soles ; the remarkable bluish infiltrated erythematous eruption on the face ; and the presence of four other skin manifestations—namely, purpura, erythema-multiforme-like lesions. cellulitis, and the specific papular infiltrate.

Case Report

The patient, a married woman aged 65, first reported to the skin clinic at the Norfolk and Norwich Hospital on July 26, 1950. She gave a history of a bullous eruption which started one month previously on the right sole, later involving the left sole and the left palm. She had had a sore throat at the onset. There was no relevant previous history.

On examination bullae up to 1 cm. or more in diameter were scattered over the soles of both feet. The dorsa of the feet and webs of the toes were quite normal. There were a few confluent bullae on the left thenar eminence. All lesions contained clear fluid at this stage. General examination revealed no abnormalities. Scrapings taken from the feet showed no evidence of fungus infection.

In the absence of a history of possible contact irritants, it was thought that the eruption was in the nature of a bullous pompholyx, and treatment was given in the form of baths of potassium permanganate, and phenobarbitone, ¼ gr. (32 mg.) thrice daily. The local treatment was changed after a week to Castellani's paint, and later to 0.5% gentian violet. No progress was made, and after a month both palms were severely involved.

In view of the discomfort and the lack of response to treatment, the patient was admitted on October 4. By this time bullae had begun to appear on the dorsa of both feet, and some haemorrhagic elements were present (Figs. 1 and 2). Glands were palpable in both axillae and groins, but the spleen was not felt.

A blood examination on October 11 showed a total leucocyte count of 79,800 per c.mm., of which 91% were lymphocytes. On November 3 her leucocytes had gone up to 123,200 per c.mm., of which 90% were lymphocytes, 4% monocytes, and 6% polymorphs. (Her haemoglobin at this stage was 98%.) No primitive cells were seen. Large numbers of smear cells were present in stained films. The platelets were not accurately estimated at the time, but the impression was that they were reduced. A sternal marrow examination on November 15 confirmed the picture of chronic lymphatic leukaemia.

A course of superficial *x* rays (to a total of 450 r) produced a dramatic effect on the bullae. After four weeks the hands were completely normal again and there were only a few small lesions on the dorsa of the feet.

During the period in hospital she developed cellulitis of the legs ; this responded rapidly to penicillin.

One week before discharge on November 24 a few scattered pinhead-sized erythematous papules had developed on the anterior surfaces of the knees and thighs. When she was seen in the out-patient department on December 7 the hands were still normal but new purulent bullae had appeared on the soles. Both feet showed a diffuse erythema

FIG. 1.—The dark pigment is not due to haemorrhage but is gentian violet.

FIG. 2.—Showing the bullous lesions that developed later on the dorsa of the feet in addition to the soles.

and both legs were oedematous and very tender as far up as the knees. Large glands were palpable in both groins. It was considered that the oedema was partly inflammatory and partly due to pressure by glands on the deep veins. A few bluish infiltrated nodules were present around the right nipple, and some pinhead-sized erythematous papules over the upper part of the sternum; there was also a diffuse erythema of the forehead. The spleen was palpable 3 in. (7.5 cm.) and the liver 1 in. (2.5 cm.) below the costal margin. A radiograph of the chest revealed the presence of mediastinal glands.

A blood count on December 7 showed: haemoglobin, 82%; leucocytes, 169,000 per c.mm. (lymphocytes 95%, monocytes 1%, polymorphs 4%).

It was decided to irradiate the glands in the axillae, groins, and mediastinum.

Progress

December 20.—The oedema of the legs had increased, and many punctate purpuric lesions were seen, especially over the shins. The most striking feature was the indurated erythema of the face, which had now spread on to the cheeks; *x*-ray treatment was prescribed for this. The leucocytes numbered 160,000 per c.mm.

January 16, 1951.—Bullae reappeared on the hands and feet. Purpuric lesions were seen on the inner aspects of the right thigh and over the shins. Subconjunctival haemorrhages occurred. The general condition had clearly deteriorated, and there was evidence of much loss of weight.

February 20.—The patient was readmitted to hospital. The facial appearance was most remarkable: a livid purplish erythema involved the whole face except for the orbit. Ringed macules, not unlike the target lesions of erythema multiforme, were seen on the trunk. Many infiltrated bluish papules were scattered over the front of the chest and abdomen. These were almost certainly specific leukaemic infiltrations, but in view of the patient's general condition a biopsy was not carried out. All superficial lymph nodes were enlarged. The spleen extended to below the umbilicus. A blood count showed: haemoglobin, 60%; total leucocytes, 265,000 (lymphocytes 97%, polymorphs 3%). The bleeding-time was 5 minutes 45 seconds; the coagulation time 3 minutes 32 seconds. The platelet count was 60,000 per c.mm.

February 23.—Pharyngitis, with systemic upset, and copious vomiting were present. The mouth was painful, with multiple ulcers. A swab from the throat showed a few haemolytic streptococci.

March 12.—She now had a gastro-intestinal upset, with haematemesis and diarrhoea. Pathogenic organisms were not isolated from the faeces.

March 20.—Her general condition was deteriorating rapidly. The skin lesions, however, were fading noticeably. The bullae on the palms and soles had practically disappeared.

March 26.—The patient collapsed with abdominal pain and died a few hours later. This was thought to be probably due to a severe internal haemorrhage. A post-mortem examination was not made.

I wish to thank Dr. A. G. Smith for permission to report this case, and Drs. A. Christie and Morgan Hall for their co-operation in the pathological investigations.

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Last year the New York State Legislature adopted an amendment excusing every pupil from "such study of health and hygiene as conflicts with the religion of his parents" (*New York Times*, January 6). This amendment, sponsored by the Christian Science Church, did not attract much attention until recently, when the New York Academy of Medicine and various teaching groups in the State demanded its repeal. They maintain that it would set back the cause of medicine and health; on the other hand the Christian Scientists state that the exemption of such children from health courses should not affect the examination questions which other children are required to answer. Their officials say that their only concern was that children of their faith whose parents request it should be permitted not to study disease symptomatology and the germ theory of disease causation. Every phase of "positive" health and hygiene is being studied by the children of Christian Scientists.

OVARIAN DENERVATION FOR OVARIAN DYSMENORRHOEA

A REVIEW OF 70 CASES

BY

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Cotte (1925a, 1925b) first drew attention to the ovary as a source of pain in some cases of dysmenorrhoea. L'Hermitte and Dupont, in 1929, and O'Donel Browne (1939a, 1939b) suggested that a painful ovary could be rendered insensitive by denervation—an operation much less severe than presacral neurectomy. O'Donel Browne has shown a cure rate of 80.9% in his series of cases.

We here present 70 cases of ovarian dysmenorrhoea treated by bilateral ovarian denervation. Resection of the ovary was undertaken if the ovary was cystic, and Gilliam's suspension if the uterus was retroverted; appendicectomy was performed in most of the cases. Histological examination of the appendix was made in cases of right-sided pain. We do not consider these additional procedures to have influenced the results.

The ages of the patients were as follows:

Age	No.	Age	No.
Under 20	2 (2·8%)	30–34	11 (15·7%)
20–24	22 (31·4%)	35–39	8 (11·4%)
25–29	26 (37·2%)	40–45	1 (1·4%)

Thirteen of the patients were unmarried. Of the 57 who were married, 33 (58%) were nulliparous and 24 (42%) parous.

Nerve Supply of Ovary.—Sympathetic fibres from the tenth, eleventh, and twelfth dorsal and the first and second lumbar segments reach the ovary via the renal intermesenteric and coeliac plexuses by way of the infundibulo-pelvic ligaments. These are vasoconstrictor. Little is known of the parasympathetic supply except that its action is vasodilator. The sympathetic supply is bilateral. Sympathetic nerve fibres may reach the ovary also by way of the ovarian branch of the uterine artery—these emanating from the presacral trunk.

Diagnosis

Site of the Pain.—In 42 cases (60%) the pain was on the right side, in 22 (31%) on the left side, and in 6 (9%) it was bilateral. It was located in the iliac fossa.

Relation to Menses.—In 28 cases (40%) the pain was premenstrual, in 21 (30%) it was intramenstrual, and in 21 (30%) it was not related. Thus in 70% of the cases pain was related to the periods.

Type of Menstrual Loss.—Menorrhagia occurred in 16 cases (23%), oligomenorrhoea in 9 (13%), and the loss was normal in 45 (64%).

Type of Menstrual Cycle.—The cycle was regular in 61 cases (87%) and irregular in 9 (13%).

The deep sensibility reflex was first described by O'Donel Browne. Bimanual compression of the ovary accurately reproduces the pain of which the patient complains. Only where this test was positive did we consider the case to be one of true ovarian dysmenorrhoea.

Operative Procedure

A midline subumbilical paramedian incision was used. The infundibulo-pelvic ligaments were divided between clamps as near to the ovary as possible so that all the nerve fibres might be included in the clamps. The divided ends were ligated with catgut and care was taken when ligating the medial pedicle that the Fallopian tube was not kinked. If the ovary tended to fall into the pouch of Douglas the ovarian ligament was shortened by a catgut stitch.

The following additional procedures were carried out: Gilliam's suspension in 12 cases (17%), cyst resection in 34 (49%), appendicectomy in 19 (27%), and myomectomy in 3 (4%). All cases in which cyst resection was done had either follicular or corpus luteum cysts.

Results

The cases were examined six weeks after operation. In the follow-up carried out the interval of time elapsing after operation varied between three years and six months. Sixty-five out of 70 replied to the questionary.

Six weeks after operation 56 cases (80%) were cured, 12 (17%) were improved, and 2 (3%) were unchanged. At a follow-up of 65 cases undertaken over a period of from six months to three years, 32 (49%) were found to be cured, 29 (44.5%) were improved, and 4 (6.5%) were unchanged.

Comment

It is shown that bilateral ovarian denervation—a simple operative procedure and one not associated with a mortality or morbidity higher than those of laparotomy—cures or greatly diminishes the pain in ovarian dysmenorrhoea.

No case was considered to have any uterine dysmenorrhoea, and in every case the infundibulo-pelvic ligaments were completely divided; yet the pain was still present to some extent after a period of three years in 33 cases (51%) of those followed up. However, in only four cases (6.5%) was there no improvement.

We believe the explanation to be that the sympathetic supply in a percentage of women reaches the ovary along the ovarian branch of the uterine artery. The fibres are therefore a part of the presacral nerve. The following case history seems to confirm this explanation.

A 1-para aged 28 complained of severe right-sided intramenstrual pain of four years' duration. Plication of the right ovary and appendicectomy had been carried out three years previously without relief. The menses were regular and the loss was normal. She was seen on August 24, 1948, and bimanual compression of the ovaries accurately reproduced the pain of which she complained. On April 22, 1949, bilateral ovarian denervation and Gilliam's suspension were carried out. She reported again 16 months later, as her symptoms were unchanged. Bimanual compression of the ovary again accurately reproduced the pain. As the ovaries were still acutely sensitive we considered that possibly the painful stimuli were reaching them via the presacral nerve along the ovarian branch of the uterine artery. Presacral sympathectomy was therefore performed on September 30, 1950. The pelvic organs at operation were normal. She reported on February 28, 1951—that is, five months after operation—having experienced no pain whatever with her periods. The ovaries were now insensitive on bimanual compression.

Right-sided Pain in Relation to Appendicitis.—Pain was right-sided in 42 cases and bore no definite relation to the menstrual cycle in 21. The condition may there-

fore sometimes be diagnosed as appendicitis. In all cases in which we performed appendicectomy, histological examination of the appendix showed no pathology. In 13 cases previous appendicectomy had produced no change in the symptoms. It therefore seems reasonable to suggest that when appendicectomy is carried out in a young woman, unless the appendix shows definite signs of acute inflammation, bilateral ovarian denervation should also be performed. This necessitates using a paramedian or Battle's incision, but does not add to the operative risk.

Resection of Cysts.—Retention cysts were removed routinely because of the difficulty in deciding which were physiological and which were pathological. Although resection of corpus luteum or follicular cysts was undertaken in 34 cases (48%) we do not consider this to have influenced the results, as every gynaecologist has seen many such cysts in insensitive ovaries.

Effect on Ovulation.—In 10 (14%) the menstrual loss was diminished after operation; in 20 (29%) it was increased, and in 40 (57%) unchanged. It will be noted that the tendency is for the loss to be increased as a result of the operation. Of the 57 married women 9 (16%) later became pregnant. We therefore assume that ovulation is not affected by division of the ovarian arteries.

Summary

Seventy cases of ovarian dysmenorrhoea treated by ovarian denervation are surveyed.

This operative treatment is undertaken only when bimanual compression of the ovaries accurately reproduces the pain.

Ovarian denervation should be practised in young women in whom definite appendicitis is not found at operation.

Relief was obtained in 93.5% of cases.

Eighteen of the cases were under the care of Mr. R. M. Corbet, and we wish to thank him for permission to include them in this series.

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Malaria has always been the greatest single medical problem for the Army in Malaya, but the War Office states that the disease rate is now under 2% in a year. New methods are being sought—for instance, "paludrine" has in the main supplanted mepacrine as a suppressive, and anti-mosquito measures are augmented by a steady flow of ingenious devices. There has been some speculation about paludrine-resistant strains, although there is no evidence as yet. Nevertheless, there was a recrudescence of malaria last summer. Dysentery and diarrhoea are present throughout the year, with a monthly incidence of between two and three cases per 1,000 troops, the early summer providing the higher figures. Skin complaints are at about three times the rate encountered in England. This may be due to jungle conditions, though in some respects the jungle shields the soldier from infective hazards met with in cantonments. What is more certainly a result of deployment in the jungle is scrub typhus, a few cases of which still occur regularly in spite of the use of clothing impregnated with a mite-killer (or more probably because of a lapse in its use). Finally, as might be expected in a country stretching almost to the equator, cases do occur of heat exhaustion, but there are not many of them. Other than the diseases mentioned and venereal disease, the sickness experience in Malaya is perhaps 15% higher than at home.

EPIDEMIOLOGY OF A HUMAN CASE OF BACILLARY DYSENTERY DUE TO INFECTION BY SHIGELLA FLEXNERI 103 Z

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It is often extremely difficult to trace the source of infection of a sporadic case of bacillary dysentery, and since phage-typing, which has proved so valuable in the epidemiology of salmonella and staphylococcal infections, is not in general use for shigella infections, knowledge of the precise biochemical and serological type of the strain concerned may provide the only guide to the possible source of infection. The point is well illustrated in the following case, in which the source of infection was traced beyond reasonable doubt to contact with an infected monkey.

On February 8, 1951, a specimen of faeces from a girl of 2 years 5 months stated to have dysentery was sent for bacteriological examination to a public health laboratory, and from it an organism giving the biochemical reactions of *Shigella flexneri* was isolated. It was agglutinated by the Standards Laboratory's *Sh. flexneri* Z and *Sh. flexneri* 103 sera, and was subsequently confirmed by the Dysentery Reference Laboratory as a typical *Sh. flexneri* 103 Z, as described in this country by Rewell and Bridges (1948). Though this organism has only once been reported from a human case of dysentery in this country (and the infection may in that case have been acquired in the Middle East), it is a frequent cause of bacillary dysentery in primates imported into Great Britain. In view of this, further investigation into the history of the case was undertaken to try to establish any possible contact with monkeys, and an interesting story was unfolded.

On February 1, 1951, the child was taken by her mother to the Pets' Corner of a large general store where there were several cages of monkeys. While watching them the child was eating an ice-cream cornet, and one of the monkeys put its paw through the cage to grab the cornet. Though the child held on to it, the ice-cream was touched by the animal, and she licked the cornet before the mother could throw it away.

Two days later the child appeared off colour, refused her lunch, and by evening had frequent motions. By February 5 the faeces contained blood and mucus, and medical advice was sought on February 7, when the child was having five or six motions a day, which was stated to be less than when she originally became ill. Apart from diarrhoea, the child had few constitutional symptoms, and difficulty was experienced in keeping her in bed. She was treated with a six-day course of succinyl-sulphathiazole, and, though two faecal specimens received on February 21 and 23 yielded no pathogenic organisms, *Sh. flexneri* 103 Z was again isolated from a specimen received on March 1. A further six-day course of succinyl-sulphathiazole was then given, and the organism was not found in subsequent specimens.

When questioned, the mother admitted to some diarrhoea herself during the child's illness, but she was

symptomless when two samples were taken, and the organism was not isolated from either.

After the positive history of contact with monkeys had been obtained the Pets' Corner was investigated with the full co-operation of the store management. The Corner was clean and well looked after, and no faeces were seen in the cages. The monkeys had all been in the store for nearly two years without any recent imports. Both the manager and the visiting veterinary surgeon stated that the animals had been healthy and had had no diarrhoea during this time.

The monkeys were arranged in the room in three main groups. In the centre of the room was a cage containing 13 monkeys, some being the common rhesus monkey, *Macaca mulatta*, and others the West African green guenon, *Cercopithecus sabaeus*. This was apparently the most popular cage. On one side was a small cage containing a mother and baby of the rhesus type, and on the other side was a row of three cages containing the same type and also the mona guenon, *Cercopithecus mona*. This row of cages was separated from the public by a breast-high iron bar with wire netting between the bar and the floor. Because of the bar, the manager thought it very unlikely that the monkey concerned could be in these cages, and, as the mother was vague regarding which cage they had been watching when the incident happened, attention was concentrated at first on the centre cage and the small side cage.

By chasing the monkeys round to startle them a number of freshly passed faeces were obtained, but no intestinal pathogens were isolated from these. It was arranged that specimens of faeces found in each cage in the morning would be sent to the laboratory. Between February 21 and March 15, 69 such specimens were examined, but no shigellae were isolated, though one sample from the centre cage yielded *Salmonella typhi-murium*. All the faeces examined were formed and none contained blood or mucus. It was then decided to take rectal swabs, and on February 16 the mother and baby rhesus monkeys and the occupants of the centre cage were swabbed, but no pathogens were subsequently isolated. However, a sample taken from a cage floor on March 15, the day it was decided to abandon this method, yielded an organism confirmed as *Sh. flexneri* 103 Z. This specimen was found with surprise to have come from the middle cage of the side row of three. Unfortunately, between the time of sampling and the isolation of the organism the five monkeys in this cage had been sent to different parts of the country, so that rectal swabs could not be obtained from them.

A further interview with the mother then elicited the fact that she was probably holding the child in her arms at the time of the incident, and subsequent examination of the protective barrier showed that, if this were so and the child had been held forward over the bar, the monkey could have touched the ice-cream cornet.

Discussion

In spite of the fact that it was too late to trace the actual monkey concerned, there seems little doubt that the child was infected by eating the ice-cream freshly contaminated by the monkey's paw; and the habits of monkeys doubtless indicate the source of contamination of the paw. As there was no time for multiplication of the organism in the ice-cream the infecting dose was presumably confined to that directly transferred from the animal's paw.

Though it has been recognized for many years that primates are naturally susceptible to infection by certain organisms of the *Shigella* genus, seldom have such animals been shown to be directly responsible for human infection. Rewell (1949) reported possible infection of a monkey-house keeper in this country with *Sh. schmitzii* from a lar gibbon, and refers to a family outbreak of bacillary dysentery in Hamburg, probably arising from pet monkeys, reported by Bach, Fulscher, and Harnack (1931). Rewell and Bridges (1949) have drawn attention to the potential danger to personnel handling monkeys during their rapid air transport to this country from abroad.

It is apparent from experience at the Dysentery Reference Laboratory and from personal communications from those in charge of monkey-houses in this country that primates can be infected with almost every type of *Shigella*; but undoubtedly the most common infecting types are *Sh. flexneri* 103 and *Sh. flexneri* 103 Z. The clinical picture of the animals varies from a rapidly fatal dysentery to a symptomless carrier state. On the other hand, infection due to *Sh. flexneri* 103 Z is rare in man. In all probability, if the child had been infected with one of the more common human *Shigella* types, such as *Sh. sonnei* or *Sh. flexneri* Z, the story of the monkey's paw might never have been obtained.

It is surprising to find that, although at least two of the monkeys in the Pets' Corner were at one time or another excreting such pathogens as *Salm. typhi-murium* and *Sh. flexneri* 103 Z, both highly infective to the species, no outbreak occurred amongst the animals. Possibly the fact that it was an established colony with no recent imports may have been responsible.

Admittedly, monkeys in this country are generally in relatively closed communities, but many such colonies are open to the public, and the measures to prevent contact between the monkeys and their visitors may not always be completely adequate to protect the one from the other. As a large proportion of such visitors are children, who are highly susceptible to both shigella and salmonella infections and who frequently on such occasions are eating titbits equally enjoyed by monkeys, a real danger would seem to exist. This could be prevented by the provision of foolproof barriers.

Summary

A case of bacillary dysentery in a child due to the rare human pathogen *Sh. flexneri* 103 Z is described, and an account is given of the investigations to trace the source of infection to monkeys, which was indicated by the fact that the organism is a common cause of dysentery in these animals. In addition to the isolation of *Sh. flexneri* 103 Z from monkey faeces in one cage of the Pets' Corner concerned, *Salm. typhi-murium* was obtained from a specimen taken from another cage.

Warning is given of the potential danger, in animal-houses open to the public, of the transmission of shigella infection from monkeys to their visitors.

Our thanks are due to Mr. B. Spencer, F.I.M.L.T., for his technical assistance; the manager of the Pets' Corner for his willing co-operation; to Mr. E. Copeland, M.R.C.V.S., for his assistance in obtaining specimens from the monkeys; and to Dr. Gedye for the specimens and clinical data from the patient.

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Medical Memorandum

Congenital Indifference to Pain

Congenital indifference to pain is a rare condition. A survey of the English and American literature since 1900 has revealed only 10 previous cases (Dearborn, 1932; Ford and Wilkins, 3 cases, 1938; Kunkle and Chapman, 1943; Arbuse, Cantor, and Barenberg, 1949; Boyd and Nie, 1949; Duncan Leys, 1950; McMurray, 1950; Farquhar and Sutton, 1951), with brief references to eight others (Critchley, 2 cases, 1934; Grain, 1949; Nielsen, 2 cases, 1949; Keizer, 3 cases, 1951).

Case Report

A girl aged 6 was admitted to Poole General Hospital in November, 1949, with a provisional diagnosis of "rheumatoid arthritis." In May, 1949, she had had a febrile illness with cough and haemoptysis which rapidly responded to a course of sulphonamide. Two weeks after recovery the right knee had become swollen, gradually subsiding over a period of three weeks. In July the left ankle became swollen and remained so; shortly before admission the right ankle had also swollen a little. Despite a limp, she remained lively and active and had never complained of pain in the affected joints. The past medical history was otherwise not relevant.

She was a shy, carrot-haired girl of normal height and weight for her age and of average intelligence. The teeth were very carious. There were extensive areas of scarring, superficial ulceration, and keloid formation on the outer side of the thighs and multiple scars on both knees. The cardiovascular system was normal; blood pressure 105/50. Her chest was clear and the liver and spleen were not palpable. There was a brawny, diffuse, non-tender swelling of the left heel and instep and a similar smaller swelling of the right ankle. There was no limitation of movement at any joint. Fundi and pupils were normal. All deep reflexes were present and equal, with flexor plantars. It was noted that she watched attempted venepuncture with amused interest, and further examination revealed that she was completely indifferent to pain over the entire body surface: pinching, pricking with pins, and firm pressure on the tendo Achilles were all tolerated without flinching or apparent discomfort. She was, however, able to distinguish between "sharp" and "blunt" without error. There was normal appreciation of light touch, heat, cold, vibration, and joint sense. There was no dysphasia, agnosia, apraxia, or astereognosis. She was right-handed.

A radiograph of the feet showed fragmentation and displacement of the epiphysis of the left calcaneum, erosion and fragmentation of the right talus, and erosion of the proximal articular facet of the right cuboid. There was a right-sided coxa vara and a congenital unfused neural arch of T 12 vertebra. Biopsy of the left calcaneum showed no abnormality. A Mantoux test to 1:100 and blood Wassermann reaction were negative. Bone structure was normal radiologically apart from prominent Harris's lines at the lower end of the fibula, tibia, and femur.

Further inquiries elicited that she had never at any time complained of or appeared to feel pain: she had often fallen flat on her face on concrete and got up laughing; while playing with other children handfuls of hair had been pulled out without her showing any concern. She had never complained of toothache, headache, or abdominal pain. Since infancy she had been a hyperactive restless child, spending her time running, climbing trees, and jumping off walls. The bony lesions of the feet were considered to be a sequel to multiple minor injuries, and with a period of strict rest in bed partial recalcification occurred. In July, 1950, she was again referred to hospital complaining of inability to "jump over a tennis net as well as usual." She was found to have a subtrochanteric fracture of the right femur with marked callus formation. The actual circumstances of the fracture could not be elicited, but again there was no complaint of pain.

Comment

In 1932 Dearborn recorded, under the title of "A Case of Congenital Pure Analgesia," the history of a man of 54 who had never experienced any pain throughout his life. He had sustained, among other injuries, a blow in the face with a pickaxe, a bullet through a finger, a broken nose, severe laceration of the knee, and a burned hand—all without apparent pain. In later life he appeared in American vaudeville as "Edward H. Gibson, the Human Pincushion," allowing the audience to stick up to 50–60 pins into his body at a time, and on one occasion to hammer a nail through his hand. Subsequent reports have all emphasized the frequency with which multiple painless fractures, dislocations, lacerations, burns, and their sequelae in the form of scarring, deformities, keloid formation, and painless osteomyelitis occur in these subjects.

Acquired indifference to pain has been described in lesions of the posterior parietal area of the dominant hemisphere, especially those involving the supramarginal and angular gyri, and is usually associated with other gross neurological defects. The possibility that congenital indifference to pain is due to a similar structural lesion of the parietal cortex must, however, remain speculative in the absence of necropsy material. Ford and Wilkins suggested that the condition was due to a "congenital dysplasia involving the neural mechanisms concerned in the perception of pain"—similar in nature to congenital word-deafness, word-blindness, and colour-blindness, in which structural lesions are known to be absent. The presence of a mild congenital word-blindness in one of their cases supports this contention.

I wish to thank Dr. J. R. Hindmarsh for permission to publish this case; and Dr. F. Parkes Weber for his advice.

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La Presse Médicale (January 12) reports that an international foundation has been created to commemorate the work of the bacteriologist Charles Nicolle (1866–1936). Among his studies were investigations on the spread of typhus by insects, on subclinical infection and carriers, and on the prophylaxis of measles by convalescent serum. The foundation has its headquarters in Paris, and it has been decided to erect a fountain in Tunis, where much of Nicolle's medico-social work was accomplished, and to establish—probably also in Tunis—a clinic and laboratories specializing in the fight against infectious diseases and those due to parasites, but especially syphilis and trachoma.

Reviews

TOO MANY PEOPLE

Human Fertility: The Modern Dilemma. By Robert C. Cook. With an introduction by Julian Huxley. (Pp. 351. £1 1s.) London: Victor Gollancz. 1951.

This book should be of particular interest to members of the medical profession, since the author discusses two problems in the creation and development of which medicine has played an outstanding part. Medical intervention in the affairs of a human population is followed by a fall in the death rate, by an uprising in the survival rate, and by a magnification of the natural increase. Indeed, it is by this fall, this uprising, and this magnification that the quality of the service that medicine renders to a population is partly assessed.

In the history of a population in which the kind of medicine that we know has found a place, a growing disharmony between the total population numbers and the total resources of the habitat develops. This disharmony is expressed in various ways, such as poverty, insecurity, and the mounting threat of starvation. Attempts to check or to reverse this process usually take the form of the eager encouragement of increased food production and of a planned industrialization of the society. But for these a great deal of time is required, and it therefore becomes necessary for the population to control its fertility and for the State to facilitate the provision of the means for so doing. The remote repercussion of medical intervention undertaken without due regard for its effects is the creation of the need for a planned population policy.

The author argues, and supports his argument by particular reference to Puerto Rico, that unbalanced and unchecked fertility is ravaging many lands like a hurricane. Nearly four-fifths of the people of the world to-day subsist near the verge of starvation. No matter what may be done to increase food production, the rate of the increase cannot equal the rate at which the human population of the world itself is multiplying. The only possible method of checking this growing disharmony is by the production of a simple, foolproof contraceptive tablet, no more expensive than an aspirin, that will produce temporary sterility when taken by the mouth. This, in the author's opinion, would offer mankind a good deal more promise of security than any world-wide agreement to outlaw war.

The author then discusses the even more debatable and complex problem of population quality. He states the argument that the innate quality of the human stock of a country such as Britain tends to degenerate progressively generation by generation. With admirable fairness he reproduces the argument that the relaxation of natural selection brought about by the intervention of the medical and social sciences in the affairs of a population must be causing slow degeneration of the stock through the accumulation of harmful mutations. He then puts forward proposals whose object is to encourage reproduction by the more intelligent and the more highly endowed. It is most desirable that members of the medical profession shall be well informed about both these matters and shall have reached, through examining the available evidence, a conclusion on their importance and on the ways in which the problems shall be tackled and solved.

F. A. E. CREW.

THE NUTRITIONAL REVOLUTION

The Nutritional Improvement of Life. By Henry C. Sherman. (Pp. 270. £1 4s.) New York: Columbia University Press. 1950. London: Geoffrey Cumberlege. 1950.

Nutrition Work in Greece. By Andromache G. Tsongas. (Pp. 67. U.S. $0.50.) Rome: Food and Agriculture Organization of the United Nations. 1951.

Teaching Better Nutrition. By Jean R. S. Ritchie. (Pp. 148; illustrated. $1.50.) Washington: Food and Agriculture Organization of the United Nations. 1951.

H. C. Sherman has spent the best years of his life in nutritional research and teaching, and in his latest book he tells the story of the development of our knowledge and its possibilities for the betterment of mankind. In the first chapter he discusses the gradual appreciation in Britain and the U.S.A. of the importance of sound nutrition for the welfare of every man, woman, and child. He then goes back to the beginnings of nutrition as a science, and describes the pioneer work of Atwater in the 'nineties on food tables and calorie requirements. There follow chapters on the progress made in each of the first four decades of the present century; energy requirements, Chittenden's protein minimum, the importance of mineral elements, and the dawn of the vitamin era are all discussed. In the chapter covering the first world war he describes the development of the idea that proteins might differ in their nutritional value according to their constituent amino-acids, and discusses the discovery and investigation of the three primary vitamins A, B, and C, but says little about the impact of the first world war on national food supplies and all that this involved. Multiplication of the vitamins and the extensive study of their biological functions in the 1920's led to the concept of optimum nutrition; the author traces the expansion of this idea throughout the 1930's. The scientific classification of rickets as a deficiency disease and its eradication from the big cities receives surprisingly little attention, however, and Sir Edward Mellanby's name does not appear at all in a bibliography which must include about 400 references.

The importance of ensuring good national nutrition was appreciated during the opening phases of the second world war, and the handling of the situation in Canada, the U.S.A., and Britain is briefly described. The latter part of the book is on rather more theoretical subjects. The nutritional aspects of the internal environment, for instance, and the relationship of nutrition to the expectation and length of life are discussed, and the implications of all this growing body of knowledge, not only for national nutrition but in the general service of man. The book closes with an appreciation of the National Research Council's recommended dietary allowances.

Nutrition Work in Greece describes the work carried out in that country by F.A.O. after the period of emergency tided over by the Unrra organization had come to an end, and shows, as it were, the practical outcome of the developments outlined by Sherman.

The author of *Teaching Better Nutrition* describes how the newer knowledge of nutrition can be got across to backward peoples, where it can do so much good. It is a pity that Hopkins's experiments in 1912 should have been given the misleading and erroneous caption, "Hopkins' discovery of vitamin A," but in general the information given seems to be correct.

These books form an interesting set of three, but to most people they will not have an equal appeal.

Sherman's is a book for the student, the F.A.O. publications for teachers and workers in the field. The triumphs they describe are impressive, but were they so difficult to win? The hard task lies ahead. Country after country is outgrowing the food it can produce, and behind the successes of the scientists stands the spectre of world famine. Technical experts in nutrition may shrug their shoulders and turn away to their pleasant jobs with the feeling that it is not their business. They may be right; in the narrow sense they *are* right. But let us hope that future historians will not look back upon the nutritional revolution and condemn those who brought it about as little men who failed to grapple, while there was still time, with the greatest crisis in world history.

R. A. MCCANCE.

FOR STUDENTS OF ORTHOPAEDICS

Regional Orthopedic Surgery. By Paul C. Colonna, M.D. (Pp. 706; 474 figures. £2 17s. 6d.) Philadelphia and London: W. B. Saunders Company. 1950.

The author is to be congratulated on producing a book which should prove of real value to orthopaedic students, both undergraduate and postgraduate. After two introductory chapters on the physiology and general pathology of bones and joints the remainder of the work is arranged regionally. For the purpose of teaching this arrangement has much to recommend it. Each chapter opens with a short section on applied anatomy followed by a description of the soft-tissue injuries, fractures, tuberculous lesions, and orthopaedic conditions of the region concerned.

By concentrating on the features which are of importance to students the author has been able to cover the whole field of orthopaedics and fractures. The illustrations, which consist of line drawings, photographs, and reproductions of radiographs, are excellent. Some of the recommendations on treatment have an American flavour which may not be entirely acceptable to students in Britain. The book concludes with two excellent chapters on orthopaedic apparatus and physiotherapy. There are few orthopaedic textbooks which satisfy the needs of the student in such a masterly manner.

J. S. BATCHELOR.

FICTION AS FACT

My Dear Holmes. A Study in Sherlock. By Gavin Brend. (Pp. 183. 10s. 6d.) London: George Allen and Unwin. 1951.

It may be a dangerous procedure to create a character in fiction. If Conan Doyle could have anticipated the great popularity which his detective hero would evoke from the English-speaking public, he might have hesitated before creating him. As it was, he appeared to get tired of his hero and killed him off, to the bitter disappointment of his public. Popular demand and perhaps economic reasons induced him to bring Sherlock Holmes into action again. It was inevitable, however, that many inconsistencies of fact would appear in a series of disconnected tales written at the publisher's urgent request.

In this attractive little book the author has attempted to reconcile many of the inconsistencies, a task which assumes that there was a factual basis behind the fiction. Those who almost believe that Sherlock Holmes was a real person will be delighted to learn the year of his birth and the approximate dates of most of his adventures; they will be interested to probe the secrets of Watson's two marriages and of his quarrel and reconciliation with Holmes. This is indeed a book which all Sherlock Holmes's fans will be eager to read. It is also a book for the philosopher to study, for here he will behold fiction treated as fact, and a myth in process of becoming a belief.

ZACHARY COPE.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received

A Textbook of General Physiology. By H. Davson, D.Sc. (Pp. 659. 45s.) London: J. and A. Churchill. 1951.

Anaesthetics for Medical Students. By G. Ostlere, M.A., M.B., B.Chir., D.A. 2nd ed. (Pp. 108. 8s. 6d.) London: J. and A. Churchill. 1951.

Massage and Medical Gymnastics. Revised by E. M. Tod, M.C.S.P., T.M.M.G. 4th ed. (Pp. 224. 16s.) London: J. and A. Churchill. 1951.

The Essentials of Virus Diseases. By P. N. Meenan, M.D., D.C.P. (Pp. 260. 20s.) London: J. and A. Churchill. 1951.

Chance and Design in Physiological Research. By G. L. Brown. (Pp. 14. 3s.) London: H. K. Lewis. 1951.

The Biochemical Approach to Biological Organization. By Professor E. Baldwin. (Pp. 20. 3s. 6d.) London: H. K. Lewis. 1951.

Studies in the Social Psychology of Adolescence. By J. E. Richardson and others. (Pp 266. 21s) London: Routledge and Kegan Paul. 1951.

Teach Yourself Management. By M. G. Frost, A.C.C.S., M.I.W.M., M.I.P.M., A.M.I.I.A., A.C.W.A. (Pp. 197. 6s.) London: English Universities Press. 1951

The Unknown Self. By G. Groddeck, M.D. (Pp. 207. 12s. 6d.) London: Vision Press. 1951.

The Bridge of Life. By A. P. Suñer, M.D. (Pp. 270. 28s. 6d.) London: Macmillan. 1951.

Medical Disorders During Pregnancy. Edited by S. Clayton, M.D., M.S., F.R.C.S., F.R.C.O.G., and S. Oram, M.D., F.R.C.P. (Pp. 341 25s.) London: J. and A. Churchill. 1951.

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Proceedings of the Third International Congress of the International Society of Hematology. Edited by C. V. Moore. (Pp. 593. $10.) New York: Grune and Stratton. 1951.

The Enzymes. Edited by J. B. Sumner and K. Myrbäck. Vol. 2, part 1: Chemistry and Mechanism of Action. (Pp. 790. $14.80.) New York: Academic Press Inc. 1951.

Leibesübungen mit Körperbeschädigten. By H. Lorenzen. (Pp. 218. M. 7.50.) Stuttgart: Georg Thieme. 1951.

Die Nervenkrankheiten. By Professor G. Schaltenbrand. (Pp. 880. M. 87.) Stuttgart: Georg Thieme. 1951.

Die Trübungsformen der Menschlichen Linse. By Dr. H. Sautter. (Pp. 139. M. 49.80.) Stuttgart: Georg Thieme. 1951.

Leitfaden der Laparoskopie und Gastroskopie. By Professor H. Kalk and Dr. W. Brühl. (Pp. 158. M. 27.) Stuttgart: Georg Thieme. 1951.

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THE EFFICACY OF B.C.G. VACCINATION

Research done as an afterthought has its pitfalls. Data which were not originally collected for a specific investigation may need to be analysed in retrospect. If, say, patients were treated with drug A in one hospital in 1946, and in 1948 the records of another hospital show that patients with the same disease were treated with drug B, can a fair comparison of the results be made? Useful information may be gained, but such investigations are full of traps for the unwary. A recent report[1] on "The Efficacy of B.C.G. Vaccination" is a retrospective comparison of this kind on a big scale. The authors, Dahlström and Difs, have studied the incidence of tuberculosis in conscripts who entered the Swedish Army between 1941 and 1944. Most conscripts were tuberculin tested. B.C.G. inoculation was offered to the 61,474 who were negative, and 36,235 (59%) accepted. Dahlström and Difs turned back to the records to study the morbidity from tuberculosis during Army service of the inoculated and of the 25,239 men who refused inoculation. This was possible because every case of tuberculosis or suspected tuberculosis in the Swedish Army is reported to the National Insurance Office. To ensure uniform assessment of the radiological findings the authors borrowed and reviewed the *x*-ray films of the reported cases (but they do not say in how many cases they were not able to see the films).

For the analysis of morbidity they have tried to distinguish those early tuberculous manifestations which could have resulted from a primary infection contracted shortly before or shortly after the date of vaccination (which developed, that is, before any protection conferred by B.C.G. could begin to operate). Under this heading come cases of primary tuberculosis arising within two months of inoculation, and pleurisy and other post-primary signs of disease arising within six months. Aware of one main weakness of the trial—namely, that the control group were those who refused inoculation and may therefore have been different in character—the authors offer evidence that the inoculated and control groups were in fact comparable at the start by recording the "early" morbidity for the two groups. During the first 60 days the incidence of primary tuberculosis in the vaccinated soldiers was 0.75 per 1,000; in the non-vaccinated it was 1.35 per 1,000. The difference being "not statistically significant," Dahlström and Difs conclude that the risk of acquiring primary tuberculosis was equal in the two groups prior to the onset of any protection that B.C.G. might afford. A similar analysis is applied to cases of post-primary tuberculosis: during the first six months the incidence was 1.52 per 1,000 in the vaccinated group, and 1.47 in the controls. It must be noted that the conclusion on equality of risk might apply to equal risk of infection in the first weeks of service, or to equal susceptibility, or to both combined: the analysis does not, nor could it, distinguish between the two. However, an investigation of the incidence of non-specific pneumonia in the follow-up period showed similar figures for the two groups.

Having found that the groups were comparable at the beginning of the study, the authors then analysed the subsequent morbidity—that is, all the cases other than the early ones. The difference between the two groups is impressive. After the first two months signs of primary tuberculosis were seen in 31 of the vaccinated (0.86 per 1,000) and 106 of the controls (4.20 per 1,000). After the first six months 46 cases of pleural effusion were noted in the vaccinated (1.27 per 1,000) and 145 in the control group (5.75 per 1,000). Post-primary pulmonary tuberculosis was seen in 15 of the vaccinated (0.41 per 1,000) and 37 of the controls (1.46 per 1,000). These differences are statistically significant, and the evidence in favour of B.C.G. appears to be very strong.

But the authors, while trying to be objective in retrospect, are not entirely so. Early in their analysis they write: "Generally speaking, the diagnosis was somewhat easier to establish in the (originally) tuberculin-negative than in the vaccinated group, being helped by the conversion from the non-reactive to the reactive state." Does this mean that a lesion in a person becoming tuberculin-positive without the aid of B.C.G. was presumed tuberculous unless the contrary was proved, but in a vaccinated person was presumed non-tuberculous unless definite proof was forthcoming? Doubtful cases amounted to 16 in the vaccinated group and seven in the controls, and the authors remark that "the smaller number in the latter group is understandable because the tuberculin reaction provided better help in making the diagnosis." This surely means that in the control group a number of cases which would have been considered doubtful had they been vaccinated were considered certain. How many there were in this

[1] *Acta tuberc. scand.*, 1951, **25**, Suppl. 27.

category is not known, but the question seriously affects the data on primary morbidity. If the authors' own objectivity were alone in question there might be little cause for concern. But the diagnosis was not dependent on them alone; they could consult only the records of cases notified as tuberculous or suspected to have tuberculosis. If a case was considered non-tuberculous by the medical officer of the unit, then presumably it did not appear in the insurance records which the authors consulted. It is conceivable that in doubtful cases a medical officer might reject a diagnosis of tuberculosis when he knew that the man concerned had received B.C.G.: such enthusiasm is not unheard of.

The authors' use of statistical analysis also tends to be misleading. When, in analysing early morbidity, they find that a difference between the two groups (as in the figures already quoted of 0.75 per 1,000 in one group and 1.35 in the other) is not statistically significant, they conclude that the two groups are *therefore* comparable or similar. This type of reasoning occurs at several points and is quite unjustifiable. If one death occurs among four patients treated with drug X and three deaths in four patients treated with drug Y, the difference is not statistically significant because the totals are small, but this does not warrant the conclusion that the effect of the two drugs is the same. The fact that other figures in the analysis provide more valid evidence of equal risk at the start does not justify the false logic in the first place.

The main defect of the analysis, however, is that, while the authors offer evidence that the two groups were comparable at the beginning of their Army service, they are not able to show that conditions were comparable during the service—that is, during the time when the men were developing signs of disease. The reader might assume at first that the proportions of inoculated men and controls were about the same in each Army unit, but on page 22 the authors write: "The incidence of vaccination probably depended more on the initiative and propaganda of the Army surgeon than on the initiative of the individual." This is understandable, and later there is evidence that in some units acceptance of B.C.G. was probably very high and in others low. In chapter 10 of their monograph the authors list "agglomerations" of tuberculosis in Army units in which at least five cases occurred among the men conscripted in the revelant year. Each of the agglomerations was in a different unit. In 16 units cases occurred only in controls; in one there were cases in both control and vaccinated groups, and in six units all the cases occurred in vaccinated men. The total of vaccinated and unvaccinated men in each unit is not given. There were three "epidemics" which occurred in vaccinated men before protection had developed, with a total of 36 cases: in the units where these occurred there were no cases among the unvaccinated men, and the assumption is that all, or nearly all, men in these units were vaccinated. Three agglomerations of cases occurred in vaccinated men alone after the date of expected development of protection. Here two explanations are possible: either nearly all men in these units were vaccinated or the vaccinated were more susceptible to tuberculosis than the controls. If the latter explanation is rejected the reader is led to form a picture, presented by the authors' own statistics, of vaccinated and unvaccinated units rather than of vaccinated and unvaccinated individuals—a different kettle of fish entirely.

With this picture of a contrast between units rather than between individuals within the units, it would be reasonable to imagine that the same medical officers who persuaded their men to accept the vaccine might also make better arrangements for medical supervision, including routine *x*-ray examinations, and, on the other hand, that in units with unenthusiastic medical officers, or inefficient medical control, few men might be vaccinated and cases of tuberculosis remain for a long time undiagnosed, with consequent infection of other men in the same units. All this is not to say that such was the case; the point is that it may have been. The authors stress that in both groups the rate of incidence of primary infections fell after the first months, and conclude, no doubt rightly, that the fall was due to effective elimination of sources of infection at the beginning. But the fall was much less in the controls than in the vaccinated, and this might be due to less effective measures in the control units. The authors state that "there is not the slightest evidence . . . that the marked fall of the risk in the B.C.G. group could have been due to more effective weeding out of sources of infection in that group," but they offer no valid support for this statement.

That these objections have to be raised is a pity, for this Swedish study is a praiseworthy attempt to extract information from past records, a complex task at the best of times. In spite of the difficulties the analysis has produced much information of great interest, and there is no doubt that the evidence, with all its defects, is strongly suggestive. Similar studies in the past have been preoccupied with the manifestations of primary disease; here post-primary morbidity has been analysed in detail, and on this the authors are especially to be congratulated. They announce their intention of analysing later results in

the two groups, and we can hope that they may then be able to consider some of the points missed in their first report. In England there is now under way a large-scale controlled trial of B.C.G. and vole vaccines under the Medical Research Council: the groups are randomly selected, and this will avoid certain errors of the Swedish investigation. It is to be hoped that those in charge of the investigation will also be well aware of the many other errors that may creep in. No investigation dealing with human beings can be perfect, but, if the success of recent well-organized clinical trials of new drugs and vaccines can be taken as a guide, it should now be possible to reach on B.C.G. a verdict much more decisive than the "strongly suggestive" which applies to this excellent report.

THE BOTTLE OF MEDICINE

In the *Supplement* this week (p. 18) we publish a summary of a memorandum prepared for the Birmingham Executive Council on conditions of general practice. The authors of this document, after drawing attention to the cost of providing free medicine for the population, suggest that "the best cure for the bottle-of-medicine habit would be a different psychological approach, such as health education and the practice of preventive medicine." Many doctors are, of course, ready to educate their patients if given half a chance, and we recently reported a meeting[1] of the General Practice Section of the Royal Society of Medicine, at which Dr. R. J. F. H. Pinsent gave an account of a year's practice, during which he had classified all the forms of treatment that he had given. At approximately half his consultations during the year he had prescribed either specific or symptomatic treatment. In 40% of cases he had given treatment by health education, by argument, and by explanation of the patient's symptoms, and in the remaining 10% he had given a placebo. Many of the doctors who spoke in a subsequent discussion, while praising Dr. Pinsent's strength of mind in refusing to prescribe a bottle of medicine so often, were for their part not inclined to do the same for a number of reasons, of which the most important appeared to be that many of their patients who expected to receive a bottle of medicine would not come at all if this were denied them. If it is true, as one was led at this meeting to believe, that over general practice as a whole health education is given to about 10% of patients and a bottle of medicine as a placebo to about 40%—that is, the reverse of Dr. Pinsent's practice—it is possible to make a rough estimate of the cost of placebos. In 1949 188 million prescriptions were dispensed in England. If 40% of these prescriptions were for a placebo, and if mist. alb. (the cost of 4 oz. of which is 1s. 7d., including the bottle and dispensing charge) is taken as typical, the annual cost of dispensing placebos would amount to £5¾ million. To a certain extent the unreasonable demands of patients who expect attention for trivial complaints may be encouraged by lack of proportion in treatment, but against the cost of unnecessary bottles of medicine has to be put the cost of the time which doctors would have to spend in bringing their patients round to a more sensible attitude towards treatment.

Although a strong case can now be made on economic grounds for limiting the bottles of medicine prescribed in both hospitals and general practice, there is no question about the usefulness of placebos in therapeutics, nor about the fact that they have in some cases a more powerful effect than known pharmaceutical agents. Wolf,[2] for instance, studying the effect of placebos on the responses of the stomach, was able to show that the circumstances in which a drug was given could alter and even reverse the expected response. For example, he was able to alleviate nausea and restore normal gastric tone with a dose of ipecacuanha in a patient suffering from sickness of pregnancy by convincing her beforehand that such would be the effect of the medicine. Another interesting example of the psychological effect of a remedy was quoted by Best and his colleagues,[3] who treated 42 patients with a complicated and alarming machine for irradiating the pituitary gland. With 18 of these patients the current was never switched on, and it was this group, receiving the same psychological treatment but no irradiation, which showed, if anything, the greater symptomatic improvement.

Individual cases in which a placebo has brought about a dramatic cure are familiar to all medical men: such cases, in fact, have formed the stock-in-trade of quacks for centuries. But are doctors justified in adopting similar methods and purposely deceiving their patients, however successful the results may be? A placebo can have the effect on a patient either of removing real symptoms and persuading him back to health or of persuading him that his imagined symptoms are caused by a real illness that can be treated with medicine. If this type of patient is treated with a bottle of medicine his symptoms, which are usually caused by anxiety and introspection, may become established and his demand for more medicine ensured.

Although the alternatives to treating a patient with a placebo cannot usefully be discussed without

[1] *British Medical Journal*, 1951, **2**, 1335.
[2] *J. clin. Invest.*, 1950, **29**, 100.
[3] *Amer. J. med. Sci.*, 1950, **219**, 276.

reference to the mentality and circumstances of the individual, there are some general rules to be observed. The intelligence of the patient is not a satisfactory guide, for reason loses its power when we think of our own health and the possibility of dying in the immediate future. In such circumstances a highly critical person may become quite gullible and, if he is enough afraid of illness and death, will trust anyone whom he believes to have the power to keep him alive. In considering the pros and cons of prescribing a placebo it is as well to bear in mind that, in spite of the great trust and esteem in which the medical profession is generally held, there is much mistrust in the minds of many people about the efficacy of its medication. Many patients are too polite to protest in the surgery, but consign the contents of their bottle to the kitchen sink, and it is certain that many packets of the iron tablets so liberally dispensed at antenatal clinics are stored out of sight in cupboards, and sometimes left in places where they may be a danger to children. Placebos should not be used for treating neurotic patients whose complaints are based on anxiety and fear of disease or for retaining the confidence of those expecting but not requiring treatment, but there are many real symptoms and diseases for which no specific treatment is offered by the *Pharmacopoeia*, and in these a placebo is often justified and can work wonders. The persuasion will be all the greater if the mixture contains a substance that will produce a subjective effect which the patient will notice. Such are the virtues of aspirin for deadening pain, of alcohol for producing internal warmth and well-being, and of turpentine for reddening the skin that it is easy to persuade patients of their efficacy in other ways undreamed of by pharmacologists. But it is a fallacy to suppose that an inactive medicine can do no harm. If prescribed in a perfunctory way for a patient needing explanation and reassurance it may increase faith in his disease rather than in the remedy, and a doctor who gives placebos in the wrong spirit may harm the patient.

THE SELECTION OF BUS DRIVERS

A good deal of evidence has accumulated in recent years to show that careful selection of bus drivers results in a reduction of the accident rate. Thus, for example, the application of selection techniques to Paris omnibus drivers is said to have reduced the number of accidents by 66% between 1929 and 1933. The Yellow Cab Company, Chicago, tested their drivers and found those classed as "unsatisfactory" on the selection tests had twice as many accidents as the "satisfactory" group.[1] In this country an inquiry was conducted by Farmer and Chambers,[2] who examined the accident records of several groups of drivers and found that accident-proneness was an important factor. They gave psychological tests to the men and found that those who failed in the tests had a higher average accident rate than those who passed; the difference, however, was not great. Bus drivers have a high reputation for safety and courtesy—the connexion between these two qualities was recognized in a recent series of posters. How are they selected?

Generally speaking, many men have the "driving" personality, and there is no serious shortage of applicants, which makes possible a reasonable degree of selection. After a careful interview by specially trained and experienced staff who review the applicant's driving history, he is given a driving test on the road. He is then required by law to undergo a medical examination before he may obtain a licence to drive public service vehicles. It is here that the examining practitioner is required to exercise not only his private conscience towards his patient but also his public conscience towards the community. Men with defective eyesight or hearing, physical deformities likely to affect driving, and those with any condition likely to cause sudden collapse—to make a list of these is a good "practitioner's quiz"—should obviously be excluded; fortunately it is rare for an epileptic to apply. Those with anxiety conditions and other psychological disturbances are also best rejected. Doctors generally drive cars themselves, but it is necessary to remember that the continuous driving of a heavy vehicle is a different proposition. The highest degree of clinical acumen is needed for these examinations, not only in obtaining a sufficiently accurate history but also in the use of that despised instrument the stethoscope.

Having emerged triumphant from his interview, test drive, and careful clinical examination, the would-be driver enters upon a period of training—and the thoroughness of this is also a vital safety factor. Once drivers are in service it is the practice to follow up their records and performance on the roads, a particularly valuable indication during the initial months of service. Many undertakings take advantage of the scheme under which the Royal Society for the Prevention of Accidents gives "safety first" awards for years of freedom from blameworthy accidents; these awards are the pride of the drivers and provide an incentive for safety.

Methods of psychological testing for accident-proneness have been developed in the United States and some Continental countries. These tests are numerous and include reaction-time, mechanical aptitude, co-ordination, vigilance, and speed judgment tests; intelligence tests are sometimes given, but good drivers are not necessarily good with paper and pencil. Their value has yet to be proved, and they are not at present in general use in this country. If, however, it could be shown that by means of the tests the exclusion of, say, 10% of applicants would result in a 20%—or greater—reduction in the number of accidents there would be

[1] Vernon, H. M., *Accidents and their Prevention*, 1936, Cambridge.
[2] *Industrial Health Research Board, Report No.* 84, 1939, H.M. Stationery Office.
[3] *Industr. Med. & Surg.*, 1950, 19, 231.

a good case for their introduction. A recent contribution to the subject is that of Brandaleone and Daily,[3] who describe the methods of selection used by the Third Avenue Transit Company of New York—personnel tests, medical, "motorability," and psychophysical examinations. These tests were introduced about three years ago, and in the case of 40 drivers they are reported as having reduced the accident rate by 40% over a 24-month period. Unfortunately, it is not stated what tests were in use before the new procedures were introduced, and clearly the more detailed assessment of a larger number of men over a longer period is required before a final assessment can be made. The present methods of selection of bus drivers used in this country appears to be giving satisfactory results, and in all this the drivers themselves deserve a measure of congratulation. They are a fine body of men.

CLOSER LINK

Of the many reports and memoranda on the association between general practitioners and hospitals published since the Health Service began, all emphasize the need for this relationship to be much closer than it is. Administratively it includes access to hospital beds where the family doctor may treat his patients, and the use of certain services obtainable only at hospitals, such as those for having radiographic examinations and pathological tests done. A less tangible feature of the relationship is that general practitioners should be welcomed in hospital wards and out-patient departments instead of, as they sometimes are, regarded as interlopers. While no dissentient voices have been raised against the principle, in individual instances reasons have been found time and again for filching a particular group of hospital beds from the care of general practitioners or for so altering hospital staffs that there is no place for general practitioners on them. Though some of these changes may have been for the good of the medical services, by no means all have been.

The Scottish Health Services Council[1] has now joined with the rest in pointing out that "there is an obvious need for a closer link between the general practitioner and the hospital and specialist services." And the committee that prepared the report had evidence of a prevalent feeling that hospital work is becoming almost exclusively the sphere of the specialist and the hospitals themselves a preserve where the general practitioner is neither needed nor welcomed. The creation of this "antiseptic barrier" dividing clinical doctors into two isolated groups is deplored by those who work on either side of it. Yet few would doubt that much needs to be done if hospital and family doctors are to be united in their efforts to treat not merely the same diseases but the same patients. Doctors abroad often look askance at how the general practitioner in Britain is, as they see it, cut off from the hospitals in his area, and are astonished to find that often enough he does not work in any hospitals.

One of the main reasons why a much closer association is needed than at present exists is given towards the end of the Scottish report: it states that the general hospital ought to be a centre of medical endeavour where general practitioners have the acknowledged right of entry and where they can meet their hospital colleagues on terms of equality. All would agree that such close association would broaden the outlook of doctors in both branches of the profession. Clinical assistantships already exist in a number of hospitals, but the Scottish report rightly goes further in advocating that the hospital structure should include a certain number of doctors engaged partly in general and partly in specialist practice. An incidental benefit of this arrangement would be that medical students could receive some of their training from general practitioners.

Once again the need for putting beds in the care of general practitioners is emphasized. Many patients admitted to hospital are suffering from conditions which their own family doctor can treat—and often does treat in the patients' homes. It is a waste of money for these patients to be treated by specialists, and admission to hospital is a break in the continuity of medical care which, however necessary sometimes, must always to a certain extent be regrettable. Again, Avery Jones has pointed out[2] that "much of the present work of hospital out-patient departments properly belongs to general practitioners."

It is to be hoped that this report will not merely be welcomed (as it deserves to be) and then left to gather dust until covered with other reports saying the same thing. The frustration to which many general practitioners bear witness is largely due to their finding it difficult to practise clinical medicine in its fullest sense. Doctors whose work lies entirely or mainly in hospitals agree on the value of consultation with the family doctor. The report indicates how these problems might be solved, but it was nearly two years ago that the Council of the B.M.A. did likewise.[3] That report also drew attention to the fact that closer contact with hospitals would enable the general practitioner to give better service to his patients, and "the knowledge of the personal and human aspect of patients in which the general practitioner is so well versed can be of enormous value in hospital treatment." If the medical services are allowed to continue to fall apart, as they will do if these warnings are not heeded, they will soon deteriorate.

STREPTOMYCIN IN OPHTHALMOLOGY

Since 1944, when streptomycin was first isolated, there has been considerable research on its use against the tubercle bacillus and against Gram-negative bacilli, neither of which are inhibited by penicillin. In ophthalmic work certain diseases are considered clinically to be tuberculous, but often without pathological or bacteriological proof, so that treatment by streptomycin in such cases may be said to be experimental. There are disadvantages in its use: bacteria quickly become resistant to it, and patients develop toxic symp-

[1] See *Supplement*, p. 17.
[2] *British Medical Journal Supplement*, July 14, 1951, p. 9.
[3] *British Medical Journal Supplement*, April 22, 1950, p. 165.

toms (nausea, skin rashes, and sometimes an affection of the eighth nerve, causing deafness and vertigo). The paper by Professor Sorsby and his colleagues (p. 119) is an interesting and instructive account of cases treated over the last three years, considered in four groups—those with definite bacteriological or histological findings, those presumed tuberculous on clinical grounds, those so presumed on indefinite grounds, and cases of tuberculous allergy. As the authors point out, most eye diseases supposed to be tuberculous are considered to be part of a general infection, so that local treatment alone could hardly be expected to be effective. On the other hand, in diseases due to Gram-negative bacilli local therapy alone should be successful.

In fact Sorsby's results show that acute conjunctivitis, and that type of corneal ulcer which is associated with Gram-negative bacilli, respond remarkably well to local treatment. In acute conjunctivitis it is sufficient to use drops (0.5 g. per ml.). But in cases with corneal involvement subconjunctival injection is the method of choice. The authors stress the point that the injection is more effective if given in adrenaline, which must be fresh. They found that subconjunctival injection is very well tolerated, and the dose recommended is 0.5 g. in 1 ml. fluid. (Each 10 minims of fluid has 5 minims 1/1,000 adrenaline added to it.) In tuberculous keratitis results were good in the three cases quoted. Streptomycin was given intramuscularly (2 g. to 5 g. daily for one or two months). In Eales's disease and in iridocyclitis clinically suggestive of a tuberculous origin results were not so good. In phlyctenular disease there are possibilities of improving cases which relapse often or do not respond to the sanatorium regime. An important fact that emerges is that only cases of proved tuberculosis can be expected to respond to streptomycin.

It is clear that success can be guaranteed in infective keratitis due to Gram-negative bacilli, but early treatment is essential to avoid corneal scars. If the diagnosis cannot be made clinically a culture should be taken at the outset of the treatment—otherwise the patient may waste valuable days using penicillin, which will do no good.

The results obtained and quoted in this paper bear out the statement made by Duke Elder and Goldsmith[1] that in ophthalmology the efficacy of streptomycin is restricted to superficial infections with Gram-negative bacilli, proved tuberculosis, and tularaemia.

B.M.A. FILM CATALOGUE

For several years the B.M.A. Film Library has been collecting a wide variety of films; it is now the largest in Britain, and contains over 200. The publication of a catalogue listing these films is therefore timely and should be of great use to B.M.A. Branches and Divisions for their meetings, to medical schools, and to other organizations. The films are clearly indexed under subjects and alphabetically, and the notes on each include a synopsis of what is shown, the author of the material, and such technical details as size, running time, and whether silent or with spoken commentary.

The value of films in medical education is beyond dispute, provided they are well chosen and presented with a suitable introduction or commentary when necessary. Experiment on how to get the most out of films has still to be carried further. Steinberg and Lewis[2] have indicated how to extend this research and have given some experimental results on teaching medical students. But there is no doubt that the present use of instructional films should be greater than it is, and anyone perusing this catalogue will be surprised at the variety of medical and surgical techniques now illustrated by acknowledged authorities. In order to maintain a high standard, the library has had every film appraised by experts for its educational value before listing it in the catalogue, and the same care has been exercised before obtaining a film for the library. The Film Committee has performed a useful service in setting out its wares so attractively in the catalogue, which may be obtained for 5s. from B.M.A. House, Tavistock Square, London, W.C.1.

"WEST INDIAN MEDICAL JOURNAL"

In spite of all kinds of difficulties, such as the explosion which recently wrecked laboratories at Makerere College and the hurricane which earlier swept across Jamaica, the new medical schools in the Colonies are making important progress. This is particularly true of the new University College of the West Indies, which has just produced the first issue of the *West Indian Medical Journal*[3] under the guiding hand of the Professor of Pathology. The journal is the offspring of the short-lived *Jamaica Medical Review*, and contains contributions from members of the Government medical services in the Caribbean as well as from the various departments of the Faculty of Medicine. Some of the articles are useful reviews (e.g., "What is Kwashiorkor?"), while others discuss the peculiarities of disease in the region, or describe scientific research in progress.

The Caribbean is a vast area, about 2,000 miles across from east to west and half as much from north to south, with about 3,000,000 inhabitants mostly scattered on small islands separated by immense stretches of sea. The aeroplane is the standard method of travel. Recently the Caribbean Council of the B.M.A., representing 425 doctors in the area, was meeting in Kingston to discuss the unification of medical services. The time is thus ripe for collaborative studies on the spread of epidemics, and the comparison of pathological processes on different islands and among the different races. The West Indies may prove to be an important natural laboratory for medical study, and with the new Faculty of Medicine at St. Andrew to lead the way results of international importance are likely to be obtained. The new journal will be there to carry them across the world.

[1] *Recent Advances in Ophthalmology*, 4th ed., pp. 262–9, London, 1951.

[2] *British Medical Journal*, August 25, 1951, p. 465.

[3] *West Indian Medical Journal*, September, 1951, 1, 1–96. Price 5s. 3d. Jamaica, B.W.I.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

PARKINSONISM

BY

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As is true of morbidity in general, we know little of the incidence of Parkinsonism in Great Britain. but with the kind co-operation of a group of practitioners in the Leeds area it has been possible to gain an approximate idea of it.

Incidence of Parkinsonism in Leeds and District

Population surveyed	485,903
Parkinsonism (all forms)	288
Approximate incidence	1 in 1,700
Approximate total in Great Britain	27,000

These figures may not be strictly accurate, but they probably represent the minimal incidence of Parkinsonism in the population. In the same survey the incidence of disseminated sclerosis was almost precisely the same—282 patients.

Aetiology

The aetiology of Parkinsonism is probably always complex. Paralysis agitans, originally described by Parkinson in 1817, is a degenerative disorder or abiotrophy of the extrapyramidal system, particularly of the corpus striatum and substantia nigra. Recent Scandinavian work suggests that there is a genetic factor in its production, but other factors have to be considered. Parkinsonism not infrequently first appears after a single head injury or following the multiple injuries of a boxer, and all neurologists are familiar with the sudden appearance of Parkinsonism after some form of emotional stress, such as is occasioned by accidents in which there was no serious physical trauma. These factors, difficult to assess, are of considerable importance in medico-legal work, but unfortunately it is rarely possible to be quite certain whether the Parkinsonism was already present before the accident or other incident. Most neurologists will have had the experience of discovering the earliest evidence of Parkinsonism in a patient being examined for some unrelated condition, who at the time of examination has no symptoms referable to his signs. As with so many other chronic, progressive, and degenerative disorders, there is an increasing tendency to take the view that paralysis agitans may be essentially a psychosomatic disorder : there are those who claim that a disordered personality precedes the physical disease, suggesting that people of drive and ambition, contained within a rigid moral framework, may develop paralysis agitans as a result of frustration. Age is certainly an important factor, and paralysis agitans is essentially a disorder of middle and later life, the sexes being affected equally.

An approximate aetiological classification is shown in the following Table, which is an analysis of 90 personal examples.

Aetiological Classification

Paralysis agitans	57%
Post-encephalitic	32%
Arteriosclerotic	4%
Syphilitic	2%
Doubtful	5%

The commonest variety of Parkinsonism is the "idiopathic" degeneration, paralysis agitans. The second commonest is that which follows encephalitis lethargica. This curious infection, thought, though not proved, to be a virus disease, spread rapidly over the world in epidemic waves from 1917 to 1925. There is some controversy concerning its existence before or after these dates, but there is no argument that it was only during this period that the disease existed on a massive scale. A considerable number of those who did not succumb to the acute phase developed Parkinsonism immediately, but in others the syndrome appeared many years later ; the longest interval in my experience is 27 years, and presumably this is not the maximum figure. Much less commonly is Parkinsonism attributed to cerebral arteriosclerosis, with or without hypertension. Examples have also been reported as the result of carbon monoxide and of manganese poisoning. Very occasionally the syndrome arises in a patient with serological evidence of neurosyphilis.

It is by no means always easy to assign any one patient to a particular aetiological group, and indeed there are some who believe this always to be impossible ; but certain features discussed below seem to be the prerogative of the post-encephalitic state, and when these appear the diagnosis of post-encephalitic Parkinsonism can be made with confidence, even though there is no history of the acute illness ; indeed, such a history is now a rarity.

Signs and Symptoms

All practitioners and many laymen are familiar with the picture of advanced Parkinsonism : the monotonous and failing voice, the expressionless face with lack of blinking, the general attitude of flexion, the tremor, which is usually asymmetrical, and the general absence of the small and repeated movements of the normal person. In its earliest stages, however, the diagnosis is difficult, particularly in the absence of tremor. The attention of the patient may be first attracted by an alteration in the handwriting, which becomes smaller and less legible. At this stage he will also notice difficulty in carrying out the finer and more skilled movements of the fingers, such as those in playing the piano. It is only rarely that disability is first noticed in the legs. On questioning, at any stage, the patient will realize in retrospect that there has been a general slowing down of all physical activity over the previous months. The tremor is familiar and characteristic, and it is rarely mistaken for anything else, but in the absence of tremor the disability, which is often limited to one arm, may be attributed to a wide variety of neurological disorders. It is only for the latter reason that early diagnosis is important so as to prevent the patient from being subjected to lumbar puncture and even more unpleasant investigations.

Among the earliest physical signs are those involving the eyes. These consist of blepharoclonus on lightly closing the lids, weakness or paralysis of convergence,

and infrequent or absent blinking except on tapping the glabella. This latter is perhaps the most constant and certainly the most characteristic sign. On tapping the glabella both eyelids blink in time with the tapping, whether this be slow or fast, and this blinking will continue indefinitely; the normal person will only blink after the first few taps. For all practical purposes this physical sign is diagnostic of the Parkinsonian state.

Oculogyric crises are highly characteristic and are pathognomonic of the post-encephalitic state. They are becoming increasingly rare. During the crisis the two eyes are suddenly turned, usually upwards, though occasionally to one side. They may turn so far up that the patient cannot see at all, and they may maintain this position for minutes or hours, and in the latter case the eyes may become painful. The attacks occur with varying frequency, but at the worst may appear every day and last for several hours. They are frequently precipitated by psychological factors. These crises are often the presenting symptom of Parkinsonism, but there are always associated eye signs and frequently other evidence of Parkinsonism, though occasionally there may be no involvement of the limbs.

Rigidity is often first detectable in the neck, a place in which it is rarely sought. After the neck the most common site for rigidity is at the wrist, and here the characteristic "cog-wheel" element is elicited by frequent passive flexion and extension of the joint. This is a most important physical sign, and it varies considerably, even from minute to minute in the earlier stages of the disease. Later, similar rigidity is constantly present at all joints, though it is always more obvious at the periphery. A tendency to propulsion or retropulsion is usually a late sign, only demonstrable when the diagnosis is all too obvious. It is important to remember that Parkinsonism, though often bilateral, is usually asymmetrical, and in many patients it is strictly unilateral for very long periods. In a considerable number tremor never appears, nor is it ever seen in the absence of the characteristic rigidity. Though often asymmetrical in the limbs, involvement of the eyes and facial muscles is always bilateral and symmetrical.

In the well-established case, but probably never as a presenting symptom, excessive salivation is frequent, particularly in the post-encephalitic patient, in whom the skin is often very greasy. To the Parkinsonian every movement is an effort, and it is usually easier for him to sit quite still than to move about; some, however, have a feeling of restlessness and an anxiety to move about, which is a practical impossibility. Not infrequently there is a complaint of pain or discomfort in the joints of the affected limbs, and stiffness or ankylosis is apt to appear in the shoulder-joints.

Apart from any question of psychogenesis, there are very important psychological aspects of the established disease. The patient finds himself living in a continuously contracting environment, in which he becomes more and more dependent on other members of the family, and small worries and problems assume unduly large proportions. Immediate emotional factors adversely affect all the signs and symptoms of the disorder—an observation usually made by every sufferer.

Prognosis

Parkinsonism is an irreversible process, and no patient has ever been cured. A small proportion of post-encephalitic cases become stationary for very long periods, and perhaps indefinitely, but all other forms of Parkinsonism are inevitably progressive sooner or later, though often with stationary phases. The rate of progress is extremely variable, but it is usually many years before the patient becomes bedridden.

Medical Treatment

Drugs of the solanaceous group have been used for over 80 years. It was pointed out about 1929, mainly by the late Sir Arthur Hall, that these drugs are most effective when given in increasing dosage up to the point at which toxic symptoms appear. This dosage is sometimes enormous; for example, the normal dose of tincture of stramonium (5 to 15 min.—0.3 to 0.9 ml.) can be increased to 100 min. (6 ml.) three times a day or even more. Tolerance has to be acquired slowly, but is lost very rapidly. If for any reason a patient who has been taking maximal doses suddenly omits his treatment it is essential that tolerance shall again be acquired slowly, otherwise serious toxic symptoms make their appearance. Occasionally when a patient omits to take his treatment a Parkinsonian crisis is precipitated, and he becomes totally rigid and immobile. This rare but alarming state of affairs soon responds to a renewal of drug treatment.

When large doses of the belladonna group are being taken there is always complaint of difficulty in reading, owing to paralysis of accommodation, and of dryness of the mouth; these can respectively be relieved by eserine drops and by adding pilocarpine nitrate to the mixture. At this point, however, medicinal treatment has become complicated, and in my experience very few patients acquire tolerance for such very large doses and then maintain them. This may well be because in the course of time drugs which at first help later become ineffective. A group of chronic Parkinsonian patients have recently been discovered, in a hospital for the chronic sick, who had been taking large doses of these drugs for many years; treatment was suddenly withdrawn, apparently with no detrimental effect. The drugs of the solanaceous group, in the approximate order of popularity, are stramonium, hyoscine, belladonna, and hyoscyamus.

About 1935 "Bulgarian belladonna" had a phase of popularity, though there was no evidence that it was, in fact, any more effective than other members of the group. The effect of these drugs is usually to give the patient a feeling of increased activity and of lessening stiffness. It is doubtful whether any of them really affect the tremor, although it has been temporarily abolished by intravenous hyoscine and other drugs. Little is really known about the mechanisms of tremor, and it has been suggested that rigidity may in some way hold tremor in check; at the same time it is only very rarely that a patient will claim that his rigidity has lessened and his tremor increased. The prolonged use of any of these drugs over a number of years carries with it the risk of chronic glaucoma.

Curare was tried about 1927, but was soon abandoned. Mephanesin ("myanesin") has been in use since 1947; it is usually given in the form of an elixir, the initial dose being 1 dr. (3.5 ml.) three times a day, which can be increased up to 4 dr. (14 ml.) taken four or five times a day. The larger doses should be well diluted with water. As with most other drugs, mephanesin may reduce the rigidity but is not likely to affect the tremor, and on the whole it has not been very popular.

Numerous synthetic drugs have been introduced for the treatment of Parkinsonism in the past few years, and the list is steadily increasing. As with the solanaceous group, all these drugs are preferably given by mouth in increasing dosage until toxic symptoms appear, and it is still important that the dosage should be increased or decreased slowly. Any of these drugs may be combined with one of the solanaceous group. The general feeling is that the new drugs are perhaps more effective than the old, and they certainly seem to produce effects more quickly.

Perhaps the most popular at the time of writing is trihexyphenidyl ("artane"), which has a pharmacological action similar to that of atropine. The initial dose is 1 mg. on the first day, increased by 1 or 2 mg. daily up to a total of about 12 mg. divided into three or four doses. Toxic symptoms may appear at or before this level, though some patients will take as much as 15 mg. and very rarely 20 mg. daily. The toxic symptoms include dryness of the mouth, nausea, dizziness, and, less commonly, blurring of vision. This drug again may produce apparent relief of rigidity and sometimes reduces salivation, though it does not appear to relieve the salivation of the post-encephalitic; its effect on tremor is very questionable.

Ethopropazine hydrochloride ("lysivane") is supplied in orange-coloured tablets containing 50 mg. of the drug, the initial dose being 50 to 200 mg., which can be steadily increased up to 500 mg. over a period of three to four weeks. Side-effects include drowsiness and dizziness, nausea, paraesthesiae, and cramp in the limbs.

"Parpanit" is supplied in tablets of two strengths, the smaller containing 6.25 mg. and the larger (parpanit forte) containing 50 mg. It is usual to start with six small tablets daily (two tablets three times a day), increasing up to a maximum of about 24 tablets a day (one large tablet is the equivalent of eight small ones). Toxic symptoms again include dizziness as well as palpitation and tinnitus.

Diethazine hydrochloride ("diparcol") has now been largely abandoned, because toxic symptoms have included mental confusion and agranulocytosis.

As with the older drugs, it is unusual to find a patient who is prepared to take the trouble to acquire tolerance for a high dosage and to maintain it. The more usual state of affairs is to find that the patient has of his own accord made a considerable reduction in the total dosage. It would often seem likely that the finally accepted dosage is not much more than a placebo. It has also been found that the antihistamine drugs sometimes benefit the rigidity and general slowness. The usual practice is to combine these drugs with one of the previously named preparations. When large doses of these new drugs are given in combination over a long period it is possible, and indeed highly likely, that toxic symptoms will appear which have not yet been described. The antihistamine drugs tend to produce drowsiness and are sometimes better limited to an evening dose only.

Oculogyric crises never respond to any of the above-mentioned drugs, though their frequency is sometimes lessened under the continuous action of amphetamine. If attacks are very frequent and prolonged, electric convulsion therapy is worthy of trial and in my experience has often proved effective. In the very rare Parkinsonian who has serological evidence of neurosyphilis antisyphilitic treatment must be instituted, but it will not be found to reverse the Parkinsonian syndrome.

Physiotherapy is probably as important as medicinal treatment. The essential part of physiotherapy is vigorous active exercises employing all four limbs, and in the very advanced Parkinsonian daily passive movements of all joints are essential. Hot baths will often relieve the disability in the joints and to some extent the general stiffness. Massage, all forms of electricity, and all emanations have no particular therapeutic value in this disease.

The psychological aspects of treatment have to be left largely in the hands of the family. There is a natural tendency to pay too much attention to the Parkinsonian, who should in fact be given every encouragement to remain at work as long as possible and to fend for himself in the house. At the other end of the scale, and particularly in the early stages before the diagnosis has been established, the patient is sometimes accused of idleness, and I have seen a case in which a nagging wife was murdered by the infuriated patient.

Surgery in Parkinsonism

The position of surgery is at present unsettled, and publicity in the lay press has often been quite irresponsible. Surgical procedures aim at abolishing tremor and replacing it by weakness or paralysis, and operations may be performed either on the cerebral cortex or on the spinal cord. Since most cases of Parkinsonism are progressive careful selection of patients for surgery is vital. Surgery should probably be limited to patients under 50 who are suffering from gross tremor which is stationary or only slightly progressive and is restricted to one arm. Such rules will exclude about 95% of all patients. It has been claimed that in the ideal case tremor can be abolished, and that the resulting paralysis is not complete, but no such guarantee can be made. I have seen a patient with a post-encephalitic tremor limited to the left hand and stationary for many years who was still able to work and to play golf and tennis; after an operation on the cerebral cortex the tremor disappeared, only to be replaced by a total left hemiplegia and Jacksonian epilepsy, with very serious and permanent disability. Operative mortality figures seem never to be lower than 17%, rising to 35% in those above the age of 50.

In assessing the value of any form of treatment in Parkinsonism it must be remembered that it has always been known that a new remedy is likely to achieve results at first, but that such benefit rarely lasts. This is not surprising, because the patient who claims to feel much better as a result of medicinal treatment rarely shows any striking objective change. It is not suggested that large doses of powerful drugs have, in fact, no beneficial pharmacological action, but there seems little doubt that much of the alleged benefit is the result of suggestion. The optimism caused by early improvement is soon replaced by dejection following relapse, and this is reflected in an attitude of hostility and resentment to the doctor—often very obvious in the patient's face. Because of the factor of suggestion, and the natural tendency of the disease to have stationary phases, the assessment of treatment is as difficult as it is with such diseases as peptic ulcer, rheumatoid arthritis, or ulcerative colitis, although, unlike these, Parkinsonism never shows phases of remission.

Finally, the Parkinsonian must be encouraged to maintain his physical and mental activities and to take an interest in the nature and dosage of the large variety of drugs available to relieve his symptoms.

RECENT HISTORY OF PNEUMONIA

OSLER CLUB SYMPOSIUM

The 99th meeting of the Osler Club, held in London on January 11, with Mr. ZACHARY COPE in the chair, was devoted to a symposium on pneumonia in Osler's time and since.

Osler's Fatal Illness

LORD HORDER began by giving an intimate and moving account of Osler's fatal illness. He said that when Harvey Cushing's *Life of Osler* appeared in 1925 he was disappointed to find that in the last few poignant pages the drama of the final stage of Osler's illness had been telescoped into a few apparently casual references. It was on December 12, 1919, that Osler, who was suffering from a prolonged and obscure disease in his chest, sent for him to come to Oxford. It was a shock to see him very ill and emaciated, in a state of extreme toxaemia, and speaking little because speech brought on a bout of paroxysmal coughing. Osler himself had jotted down for his information, in that terse fashion of his, some pencilled comments on his own condition. Seven days previously the chest had been punctured and a little serous fluid drawn off without any relief of symptoms. Lord Horder postulated the presence of an interlobar empyema, and the puncture was repeated, using the longest needle procurable at the time. The same sort of fluid was forthcoming and that only in small amount. The condition remained relatively unchanged for another week, so that he made up his mind that something further should be done by way of exploration. A couple of extra long needles were made, Osler readily agreeing to the exploratory "séance." The first puncture was negative, but the second was successful, and when the stylet was withdrawn Osler himself said, "You've got it, my boy." Between 4 and 5 ml. of stinking pus was withdrawn. On the following day Charles Gordon-Watson drained an abscess cavity. The drainage, never very copious, ceased three days later. No further collection of pus was revealed by a second operation. Four days later the end came in dramatic fashion. He (Lord Horder) had talked with Osler in the morning, and had then gone to lunch downstairs, when the nurse called him quickly, and on going upstairs he found that the dressings and the bed were soaked in blood. The sepsis had opened up the wall of a small vessel in the upper lobe of the lung, and Osler died a few hours later that day.

A study of Osler's last illness threw little if any light on the subject of pneumonia in general. The fact that the pus contained Pfeiffer's bacillus was no more proof that the original disease was an "influenzal pneumonia" than the fact that the onset of the disease occurred during a period of fairly high influenzal incidence. All that could be said was that the disease might well have come into the category of what was to-day called "atypical or virus pneumonia," an unfortunate introduction into the nomenclature. Nor did he much favour the term "pneumonitis," though there was more to be said for it. Even in a severe epidemic of influenza it was more helpful to label the condition "influenza with pneumonia" than to call it "influenzal pneumonia." The critic might ask what a name mattered, but it did matter how words were used, because words determined subsequent thinking. The tendency to stress the lung condition so as to give it a predominant place in the nomenclature was probably due to the fact that, both clinically and histologically, the lung lesions declared themselves while yet the search went on for causative agents in the great majority of virus infections. This tendency should be resisted. With more research and some forbearance the answer would be unfolded.

As long ago as 1887, in an editorial summary of a report on pneumonia in the hospitals of New York and Boston, Osler said that the disease had come to be known as a specifically self-limited disease, and the only rational treatment was the expectant one. He added, however, that to the next generation the symptomatic and expectant plan of treatment then in vogue would appear crude and unscientific. Osler's prophecy had been fulfilled, and so no doubt would be a further prophecy that the generation next to ours would regard as crude and unscientific the nosology at present used with respect to pneumonias in the textbooks to-day.

The Advent of the Sulphonamides

Sir LIONEL WHITBY followed with a succinct account of the discovery by Domagk and his assistants at Elberfeld of the anti-streptococcal activity of an azo dye containing a sulphonamide group. Domagk's compound, known as "prontosil," was patented in 1932, but the experimental results were not published until 1935, and these were followed by clinical reports in German literature concerning work which had been going on in the trial period. Prontosil was a water-insoluble basic azo dye (sulphamido-chrysoidin) suitable for oral administration, from which an acid dye known as prontosil soluble was developed. It was early suggested and later proved that this complex molecule of sulphamido-chrysoidin owed most of its virtue to the fact that it was reduced in the body to *p*-aminobenzene-sulphonamide, now known as sulphanilamide.

As a result of a great deal of research there eventually emerged so far as pneumonia was concerned, and in historical order, sulphapyridine (at first known as M. & B. 693), sulphathiazole, sulphadiazine, sulphamezathine, and sulphamerazine. The first of these was synthesized by Ewins and Phillips, of May and Baker, Ltd., and was proved to have great therapeutic value against pneumococcal infections in mice. Clinical confirmation in the human subject soon followed, first in a few cases reported by Telling and Oliver 13 years ago, and then by Evans and Gaisford, who in a Birmingham municipal hospital in that year treated 100 cases of lobar pneumonia with a mortality of no more than 8%, whereas the control series had a death rate as high as 27%. From even this small experiment it was clear that the disease which in the days of Osler could be treated by no more than palliatives, stimulants, sedatives, and careful nursing, and later by a laborious and expensive serum routine, could now be easily and cheaply controlled.

Sir Lionel Whitby gave one or two personal anecdotal recollections of those wonderful years. It was the intrusion of a good dinner which led to the feeding of a batch of mice with sulphapyridine at a rather late and unpopular hour—indeed, well after midnight. This batch was the first to exhibit a survival rate of 100%. Thereafter in all assays the technique was so altered as to contain a night dose, and all who recalled the time when the "sulpha" drugs were used widely for the treatment of pneumonia would remember that this rule was carried out at the bedside with dosage four-hourly day and night.

Sulphapyridine was handicapped by the intense vomiting it caused, which led some who owed their lives to the drug to declare that they would prefer to die rather than endure the treatment again. Thus sulphathiazole, not much more active but far less toxic than sulphapyridine, came to replace the latter as soon as it had been rediscovered. Sulphathiazole was in actual fact found at the same time as sulphapyridine when mouse tests were being carried out, but there was a tendency to pass it over, since in the animal it seemed to have little or no advantage over sulphapyridine—a finding which was due to rapid excretion and therefore low blood concentration.

It might be said as a historical fact that the sulphonamides, from sulphapyridine to sulphamerazine, held the field for the specific treatment of pneumococcal pneumonia until penicillin came to be sufficiently plentiful for everyday use. Even to this day one or other of the potent and relatively non-toxic sulphonamides could still be regarded as an indispensable drug.

Changing Clinical Aspects

Sir ADOLPHE ABRAHAMS said that he was told that the modern medical student rarely saw a case of typical lobar pneumonia. Unhappily a "superannuated physician" had had ample opportunity for such clinical observations. But

was there in fact a remarkable reduction in the present-day incidence of lobar pneumonia? Had the type of case changed, and had the treatment by sulphonamides been responsible for the change? Then what about all this business of virus pneumonia or pneumonitis? He was not in a position to judge. "Old dogs do not learn new tricks." In his view lobar pneumonia received in many circles an entirely wrong nomenclature. He was taught—not by Lord Horder—that pneumonia was a disease of the lungs, a misconception which he had never been able to dispel. Osler rightly put pneumonia in his section of diseases due to bacterial infection; yet modern textbooks of medicine put it among the diseases of the respiratory organs. Pneumonia was no more a disease of the lungs, although respiratory symptoms predominated, than typhoid fever was a disease of the intestines.

During 2½ years in the first world war he (Sir Adolphe Abrahams) saw 558 cases of lobar pneumonia from onset to termination. In nearly every case the disease began with a rigor. Temperature was generally of the order of 102–3° F., rarely higher. The pulse–respiration ratio, upon which clinicians were very emphatic, was raised. Physical signs in 80 or 90% of the cases occurred within the first four days. Physicians with exceptional experience developed a flair for the recognition of early physical signs; they did not wait for such features as dullness at the base or even bronchial breathing, but there was a queer little catch in the breath which they recognized. In only 12 of his cases were physical signs entirely absent throughout the illness. The sputum was generally of the so-called rusty type. In something over 10% of the cases sputum was entirely absent. Other features worth mentioning were herpes, which Hippocrates had observed, and which denoted a good prognosis, abdominal pain (severe in 31 of the 558 cases), and thoracic pain (almost invariable, and not always on the same side as the physical signs, and more frequently on the right than on the left). The mortality had been 10.9%. The only complication of any real significance was empyema, the incidence of which was over 20%. Other complications were pericarditis, meningitis, arthritis occasionally, and, he supposed, infective endocarditis, but these were very few indeed.

As for prognosis, one of the features of lobar pneumonia was that some who were almost moribund recovered and sometimes a comparatively benign case running a good course suddenly collapsed and the patient died. The fact that the only treatment in those days was expectant and symptomatic did not prevent people from trying all sorts of remedies. It was a commonplace for practitioners to write to the medical journals stating that they had been in practice for 20 years and had seen 15 cases of lobar pneumonia all of which had recovered in consequence of a particular treatment. People who used vaccines produced figures which to a certain extent were convincing. In his own series he had at one time 70 consecutive cases without a death. Had he adopted some form of special treatment, the more fantastic the better, the conclusion would have been irresistible that his treatment had had something to do with it. At one time brandy was regarded as a sort of specific. On the other hand, the London Temperance Hospital then gave alcohol only to patients practically moribund, with the result, of course, that their statistics worked out very much to the detriment of alcohol. Oxygen was used, but more for the benefit of relatives than of the patient. But the treatment in those days boiled down to good nursing, fresh air (if he himself had any choice in the matter he had his patients in the open air), and, above all, sedatives to induce sleep. In his experience 70%, he thought, would have recovered whatever was done; between 20 and 30% would have died whatever was done. There remained 5 or 10% in which skilled treatment and nursing might just have turned the scale. He was always impressed by Leonard Williams's dictum that pneumonia was best treated by faith, hope, and charity—faith in *vis medicatrix naturae*, hope for the absence of complications, and charity towards those who differed from you.

Various Experiences

Sir ALEXANDER FLEMING recalled a senior physician to whom he was once clerk whose chief treatment for pneumonia was ice packs. Unfortunately, he had a junior who did not believe in ice packs and put on poultices—a confusing situation. Sir Alexander was told that they did not see pneumococcal pneumonia in hospital now. Sulphonamides and antibiotics were given outside, and the hospital got only the cases where these agents failed. The cases that came to hospital were sometimes amenable to "aureomycin" or "chloromycetin," and then they were called virus pneumonia. "I do not know what virus pneumonia is, but it is quite a nice name, anyway." Dr. W. R. THROWER, who was associated with the work in the laboratories of May and Baker, gave an account of his first case treated with "693." On May 16, 1938, he was presented with a box of the tablets and forgot about them, but two days later a case of lobar pneumonia in a man aged 45 was presented, and he decided to see what these tablets could do. It was not known how much to give, nor how often, nor how the drug acted. A very tentative start was made by giving 0.5 g. four-hourly. The dose was repeated throughout the night. The next morning the patient was no worse, perhaps better, but by the afternoon there was undoubted improvement. The following morning, which should have been the morning of crisis, the patient was sitting up and asking for food. Mr. G. H. COLT described his own experience as a patient with double pneumonia at the time of the first world war. The great help was nursing. The V.A.D. service, which produced hot meals at all hours of the day and night, helped tremendously.

Dr. ALEXANDER CAWADIAS spoke in appreciation of Lord Horder's insistence on careful nosology and upon the natural history of disease, to borrow a term from Sydenham. The natural history of pneumonia was, of course, first described by Hippocrates. One of the best descriptions in modern times was by the French nosologist Grisolle. Dr. Cawadias agreed with Lord Horder in his objection to the term "influenzal pneumonia." Influenza was in one morbid category and pneumonia in another. Concerning the history of treatment, he mentioned that meted out to an early Empress of Austria in the eighteenth century. It was reported that she had cough, sputum, and pain. The physicians were called in and bled her 3 or 4 pints. She was no better, and they bled again, 5 or 6 pints, and, as there was no improvement, they came next day and bled her again, and it was reported that "notwithstanding the active bleeding, the patient died."

Mr. DICKSON WRIGHT mentioned post-operative pneumonia, of which, he said, there were two kinds, one occurring immediately after operation and the other later. The second was the more serious in its effects. The respiration rate was high, the patient became very toxaemic, and there were mental changes.

The CHAIRMAN (Mr. Zachary Cope) mentioned that he started his career as house-physician to David Needham, who was one of the advocates of ice packs for pneumonia. Needham was a most conscientious physician, and thought there was scientific proof that the pneumococcus did not thrive so well if the temperature was a little lower than that of the body, so that the external application of an ice pack would reduce the temperature inside the chest to the required degree. It was extraordinary that so conscientious and scientific a man should adopt so pseudo-scientific an attitude. Post-operative pneumonia used to be attributed to the anaesthesia, but that was a misplaced judgment, because it had been proved again and again that pneumonia developed even after a local analgesic, when there was no infiltration of any substance into the lungs and the operation did not interfere in any way with the diaphragm.

Mr. Cope added that there were two or three medical evenings which were indelibly imprinted on his memory, and to these would be added the meeting of that evening, with the three brilliant opening addresses, the first of them, full of clinical wisdom, by a man who had just celebrated his 81st birthday.

It was announced that Dr. Carlyle Lyon had presented the Club with certain books, including a volume of the *British Medical Journal* for 1886 which contained some of Osler's earliest writings, his Cartwright lectures on the blood corpuscles.

MEDICINE IN UGANDA

[FROM A SPECIAL CORRESPONDENT]

The annual clinical conference of the Uganda Branch of the B.M.A., held from December 7 to 9, 1951, in the Makerere Medical School at Mulago Hospital, by courtesy of the dean, was attended by many Uganda members, by representatives from Kenya and Tanganyika, and by visitors from the United Kingdom. The president of the branch, Dr. A. W. WILLIAMS, opened the proceedings with an account of the history of Mulago Hospital and the growth of the medical school.

History of the Hospital and Medical School

The Government hospital at Mulago, founded in 1913 as a venereal diseases treatment centre, had grown from a collection of mud-and-wattle grass-roofed wards to a 650-bed general hospital, accommodated in pavilion-type wards spreading down the slope of the hill. Proposals for new buildings had twice come to nothing, in 1939 and in 1946, but within the last few months a site had been cleared on which it was hoped a new hospital would be built.

The medical school, which had begun as a departmental training school of the Uganda Government, had admitted its first four students in 1924 under the first medical tutor, H. B. Owen, later principal of the school and medical superintendent of Mulago Hospital. Students from outside Uganda had been admitted in 1930. The course, at first lasting only four years, including premedical studies, without anatomical dissection, midwifery, preventive medicine, or more than the most rudimentary pathology, had developed by stages to a seven-year course with a content similar in all respects to those given in the medical schools of Great Britain. It catered now for students from Kenya, Uganda, Tanganyika, Zanzibar, and Nyasaland, who, on qualifying as holders of the Diploma of Medicine of Makerere College, became medical practitioners licensed to practise in East Africa. Well-equipped preclinical departments and a fine medical library had grown up, and there were now vigorous clinical and pathological departments at Mulago Hospital staffed jointly by members of the Colonial Medical Service and of the Makerere College clinical departments.

In tracing the growth of the hospital and school, Dr. Williams paid tribute to Uganda's voluntary hospital at Mengo and its staff, who under the late Sir Albert Cook had pioneered Western medicine in East Africa; and emphasized the indebtedness of the school to the many Colonial Service medical officers, pathologists, and specialists who had served at Mulago in the last 35 years.

Sir HENEAGE OGILVIE then spoke on the surgeon's part in the fight against cancer, and discussed the place of radiotherapy and chemotherapy in the treatment of malignant disease. In answer to a question whether East Africa should press for a radiotherapy centre, he said that the cost would be high and that he felt that the money could be more usefully spent in other ways.

The president of the Uganda Branch then opened an exhibition prepared by the major pharmaceutical and medical supply firms, the first seen in Uganda, and one which was very much appreciated by those present.

Indolence or Illness?

A discussion took place on "What are the economically important diseases of Uganda?" Dr. J. M. CALDWELL gave some figures compiled from the returns made by the larger employing concerns in Uganda, and dealt especially with malaria, respiratory disease, tropical ulcer, and injuries as causes of loss of working hours. Tropical ulcer was a disease of the agriculturist, and in such folk correlated closely with the figures for total injuries, but this was not seen in factory workers. It was regrettable that the largest employer in Uganda, the Government, made no returns. Dr. Caldwell stressed the great importance of respiratory diseases and malaria as causes of morbidity, and Dr. R. G. LADKIN supported this by an analysis of the causes of morbidity in persons attending rural dispensaries in the regions round Kampala. The analysis covered over 250,000 out-patients. He pointed out that attendance at rural dispensaries was the nearest thing to a general-practitioner service available to Africans in Uganda. Although malaria (165/647) was the most frequent cause of admission to beds, in dispensaries it was closely followed by pneumonia (159/647), and as a cause of attendance respiratory diseases far out-topped malaria. Injuries, local infections, and surgical emergencies were the next most frequent conditions, followed by diarrhoea and dysentery, burns, pyomyositis, and gonorrhoea (all in the region of 15–45/647). Arthritis, whooping-cough, and tropical ulcer were the remaining major causes of invalidism. Dr. Ladkin then analysed the factors contributing to the high incidence of pneumonia, and concluded that the incidence was low in sparsely populated rural areas, increased considerably in areas of higher population density, and occurred in epidemic forms in overcrowded areas. It was one of the most important diseases of Uganda.

Mr. PAKENHAM-WALSH, of the Uganda Company, speaking as an employer of African labour, expressed the view that all this information hardly concerned an employer of unskilled African labour. Disease was not a cause of low production. Too much emphasis was now placed on the need to raise the standard of health and living in order to obtain a greater output per day. Since the war, conditions of health, housing, and food had improved and absenteeism had been reduced, but work output had actually fallen. By custom, agricultural work ceased at noon or when the task appropriate to such working hours was completed, and, while disease might make a man slow in completing his task, the healthy man did no more. In a labour force of 850 men in the last 12 months absenteeism from sickness was only 0.9% and absenteeism from other causes was only 1.9% as against 30% before the war, when no food was issued. The more serious diseases of Uganda were indolence, established custom, and lack of economic pressure.

An animated discussion followed these papers. The question of incentives was raised, and one suggestion for reducing invalidism was the supply of cheap waterproof clothing. Mr. Pakenham-Walsh's experience was supported by many present.

The Absence of "Stress" Diseases

On the following morning a clinic was held by the staff of the medical division of the hospital. Cases were shown by Dr. A. W. Williams, Dr. P. W. Hutton, Dr. A. B. Raper, and Dr. H. C. Trowell.

Dr. J. H. SHELDON then described his experiences with A.C.T.H. and cortisone in clinical medicine, and went on to discuss their relevance to local conditions. He was fascinated by the fact that all the diseases for which they were frequently used in temperate regions, rheumatoid arthritis particularly, were absent or very rare in Uganda. He hoped that research would be directed to the elucidation of the problems presented by this disparity. It seemed that the African response to stress was abnormal; or was it normal and the European reaction abnormal? Did diet play a part? It seemed possible that a deficient diet might not provide the necessary materials for the elaboration of steroid hormones and that the frequency of enlarged adrenal glands in Africans was an indication of an attempt to make good this failure.

Epidemiology of Schistosomiasis in the West Nile District

Dr. G. NELSON then described his survey of schistosomiasis (Mansoni) in the West Nile district, where the

Nile leaves Lake Albert and meanders on its way to the Sudan. The results of large surveys suggested that the infestation was spreading downstream from the lake. The incidence in children in the upper reaches was extraordinarily high, but the effects seemed minimal, and he considered that increasing malnutrition due to extended use of the protein-poor cassava was a much more important source of ill-health. He had found evidence of periodicity: in regions where there had been a high incidence in previous years the incidence was now much less. The infestation caused little apparent effect, save perhaps in children; the incidence of anaemia, splenomegaly, and abdominal symptoms was no greater in infested patients than in those uninfested. He presented in many maps and tables the results of this survey.

In the subsequent discussion Dr. LADKIN suggested that poor rainfall, resulting in unflushed pools, might account for the spread of the disease rather than the dispersal of infected snails on floating vegetation in the Nile. He described the failure of the rains in 1942–3 with consequent famine in the area, which, he thought, might have upset the ecological balance and led to spread of infestation. He agreed that cassava was a greater menace than the schistosome. Dr. Ladkin's views were supported by several speakers, but no one could explain how pools teeming with snails one week could be so free of snails one week later and in the absence of flushing. Dr. Nelson's comments on the absence of signs and symptoms due to *Schistosoma mansoni* infestation received wide support.

Uterine Tone and Pregnancy Anaemia

Professor W. C. W. NIXON then discussed the problem of abnormal uterine activity in labour, illustrating his points with records of the uterine contractions, including some taken during his visit to Uganda. He dwelt on the relevance of this work to local conditions where difficult labours and rupture of the uterus were frequently seen, and he speculated on the cause of the hypertonicity he had found in the African uterus.

Dr. J. M. VAIZEY then discussed some 66 cases of anaemia in pregnancy studied in Eastern Uganda. By European standards all the 2,020 pregnant women studied were anaemic, but he had made a special study of a group with haemoglobin levels of less than 6 g./100 ml. Most of these showed a macrocytic hypochromic anaemia which responded to good food and iron, with deworming if there was ankylostomiasis. But neither helminthic infestation nor malaria accounted for more than a small proportion of cases. Some had developed their anaemia very suddenly and had not responded even to intravenous iron. There were no cases resembling tropical macrocytic anaemia. He felt that malnutrition played an important part, most of the cases coming from an infertile area where cattle could not be raised. In the discussion which followed, the question of mineral deficiencies in the soil was raised, but analysis had not demonstrated any particular deficiency or excess.

Preventable Blindness

The following morning a clinical demonstration was given by the staff of the surgical division of the hospital. Cases were shown by Mr. I. W. J. McAdam and Mr. H. J. Croot, and Mr. D. P. Burkitt demonstrated artificial legs in various stages of construction, made locally from plasticized asbestos sheet. The legs were very light, unaffected by moisture, ant-proof and fire-proof, and cost £1 each.

The problem of blindness in Uganda was the subject of a paper by Dr. A. J. BOASE, who discussed some of the commoner causes. There were no reliable statistics, some putting the incidence of blindness as high as 1% of the population (5,000.000). Corneal blindness from keratoconjunctivitis and from trachoma accounted for some 80% of the blind seen at Mulago Hospital; these cases were avoidable. Contrary to the general belief, senile cataract was much the same in incidence as elsewhere, but the common occurrence of symmetrical cataract in young adults, probably hormonal or metabolic (not diabetic), called for elucidation, as did also a not uncommon primary optic atrophy assumed to be of viral origin. "Hetrazan" promised much in onchocercal disease of the eye: a cited case, blind from bilateral papillitis, with the aqueous of each eye teeming with microfilariae, had made a dramatic recovery. The possibilities of surgery were shown in the case of a man who had been blind from trachoma: bilateral tarsectomy followed by bilateral penetrating keratoplasty had removed all signs of trachoma and restored vision.

African Children

Dr. R. F. A. DEAN then described his observations on African children. At the outset of his work he had been struck by several details which suggested a lack of masculinity in the physique of the boys, particularly in those from the wealthier strata of African society. He found that the older schoolboys (16 to 22 years old) had very little facial or bodily hair, and an unexpected smoothness of outline; 6 out of 180 had gynaecomastia. Investigations of a group of boys 6 to 15 years old confirmed the findings of an intersexual type of physique; measurement of hand bones showed development proceeding in advance of a U.S. standard (although height and weight were below U.S. standards) and bodily proportions that were more nearly feminine than masculine.

Examinations of younger children (6 months to 3 years old) showed that they were developing poorly. It was from this age group that the majority of cases of kwashiorkor were derived. There seemed no doubt that protein deficiencies in the diet were responsible for the onset of this disease, and high-protein diets had been used successfully at Mulago Hospital. Up to 125 g. milk protein had been given daily. In the serum of 45 relatively uncomplicated cases the treatment had brought about rises in the concentration of total protein, albumin and globulin, and in the levels of many enzymes. All this was consistent with the relief of protein deficiency. There had also been a big rise in serum cholesterol. Attempts at increasing the amount of dried skimmed milk in the diet had disclosed an unexpected intolerance of carbohydrate. This extended to lactose, sucrose, glucose, and maltose, and was a severe handicap in therapy. One of the principal items in the local diet was the cooked banana or plantain, which contained very little protein. When this was given alone to experimental animals they developed fatty livers and changes in the pancreas. The youngest animals seemed most affected. In some experiments methionine added to the banana diet had seemed to prevent the development of the fatty livers, but there might be other deficiencies. Success in treatment of kwashiorkor might have been due partly to methionine, and a further trial of this amino-acid was in progress.

Many children probably passed through a period in which they suffered from kwashiorkor in an unrecognized mild form. They might, however, sustain liver damage which did not completely clear up, and which might underlie the high incidence of various liver diseases known to afflict Africans. It seemed possible that biochemical changes due to the disease might be responsible for many unexplained differences between Africans and Europeans. An upset cholesterol metabolism might, for instance, lead to the abnormal production of steroid substances and therefore to the development of intersexual characteristics and to unusual response to "stress." It was emphasized that the connexions between the pathological states found in the various age groups were so far tenuous and theoretical, but the speaker believed that a single pathology, having its origins in dietary insufficiency in infancy, was an economical and acceptable hypothesis.

The meeting was closed by the president, who thanked the speakers. He hoped many would return to the next annual clinical conference. This was the second held by the Uganda Branch, and there was an average attendance of over 50 members at each session, and over 70 members and guests had been present at the dinner. The Uganda Branch had a widely scattered membership, although the largest body of members was in Kampala; the purpose of

the annual clinical conferences was to give the up-country members a chance to attend meetings, and the council of the Branch were gratified by the large number who had attended.

ADDENDUM

BY

Professor W. C. W. NIXON

For the first time in the history of Makerere Medical School external examiners from the United Kingdom took part in the examinations in the final-year subjects. Sir Heneage Ogilvie (Guy's Hospital) examined in surgery and anatomy, Dr. J. H. Sheldon (Wolverhampton) in medicine, and Professor W. C. W. Nixon (University College Hospital) in obstetrics and gynaecology. Professor Esther Killick (London School of Medicine for Women) travelled with the group and examined in physiology.

The Uganda Branch of the British Medical Association arranged to hold its annual general meeting after the examinations so that the above visitors could participate. The organizers of the meeting are to be congratulated on the choice of subjects and the number of members attending. Ample opportunity was given to the visitors from home to examine patients in the wards of Mulago Hospital. Mengo Hospital, founded in 1844 by the late Sir Albert Cook, was also visited. There we were pleased to meet Miss Margaret Basden, who is working temporarily at "Mengo," having recently retired from the staff of hospitals in London.

The visitors from Britain made new friends, exchanged ideas, and acquired fresh knowledge. By the meeting being held at Makerere College members were given the chance of seeing the way this medical school is developing and how it was achieving its aim to train Africans as doctors. Its staff is to be congratulated on the way it is handling this task and deserves all the support possible from colleagues at home.

There can be no doubt that the Uganda Branch of the B.M.A. is one of the most active and thriving overseas.

ORDER OF ST. JOHN OF JERUSALEM

The *London Gazette* has announced the following promotions in, and appointments to, the Venerable Order of the Hospital of St. John of Jerusalem:

As Knights: Major-General F. H. Mitchiner, C.B., C.B.E., T.D., Lieutenant-Colonel C. G. Booker, M.D., Major E. S. B. Hamilton, *M.C.*, M.B., F.R.C.S., Captain R. V. Steele, M.B., Drs. K. S. Maurice-Smith, F. L. Newton, N. Manson, C.B.E., and F. L. Richard. *As Commanders (Brothers):* Sir William Coates, K.C.B., C.B.E., D.L., V D., T.D., F.R.C.S., Surgeon Captain A. McCallum, O.B.E., M.D., Brigadiers W. H. du Plessis, O.B.E., M.R.C.S., L.R.C.P., and T. W. Davidson, M.B., Colonels C. H. S. Redmond, T.D., M.B., and O. L. Shearer, C.B.E., M.B., Lieutenant-Colonel G. G. L. Stening, M.B., Drs. J. T. Whitley, O.B.E., M. C. Lavin, K. E. Dowd, F. C. Middleton, M.B.E., C. R. de C. Sadler, and W. R. Russell, and Mr. F. W. Law, F.R.C.S *As Officers (Brothers):* Major-General F. K. Norris, C.B.E., D.S.O., M.D., Lieutenant-Colonel F. K. Mugford, M.B., Captains G. R. H. Wrangham, M.R.C.S., L.R.C.P., and J. C. Mead, M.B., F.R.C.S., Drs. F. MacLagan, A. D. D. Broughton, M.P., E. M. Dearn, G. E. Sawdon, W. J. Griffiths, F. C. O'Mara, T.D., G. W. Gale, R. P. Myers, W. P. Warner, C.B.E., D.S.C., W. W. King-Brown, J. G. F. Hosken, R. W. Harte, D. A. Bathgate, N. C. Speight, C.B.E., T. H. Pettit, E. C. Brewis, and E. A. Daley, Messrs H. B. Stallard, M.B.E., M.D., F.R.C.S., S. L. A. Manuwa, O.B.E., M.D., F.R.C.S., and G. W. A. Keddy, M.D., F.R.C.S. *As Associate Officer (Brother):* Dr. J. Cohen. *As Serving Brothers:* Lieutenant-Colonel H. B. Porteous, M.B.E., M.D., Majors M. S. Harvey, M.B., S. Newsom, M.B., F.R.C.S., H. C. Stewart, M.D., M.R.C.P., and T. MacF. Wilks, M.B.E., T.D., M.R.C.S., L.R.C.P., Captain J. N. L. Thoseby, M.B., Drs. S. S. Datta, M. Y. Paget, A. Armit, E. E. Kath, J. Gregoire, J. Howie, F. F. P. Malcolm, F. A. Brown, G. E. J. Porter, W. E. Hadden, C. Wilson, A. Russell, J. A. Lees, O. H. D. Oliver, R. G. Eastwood, J. Walker, C. W. Walker, E. I. Puddy, H. V. Crabtree, V. G. Best, W. McLaren, J. K. A. Beverley, D.S.C., J. H. D. Edwards, and W. A. Fleming. *As Associate Serving Brothers:* Drs. A. Rabinowitz and M. Franks. *As Serving Sisters:* Drs. Roberta B. Nichols, Dorothea F. Coles, Florence E. Stewart, and Hilda Carmichael.

Reports of Societies

VITAMIN B_{12}

A conference on vitamin B_{12} was held by the Nutrition Society on January 5 at the London School of Hygiene and Tropical Medicine. Professor L. J. WITTS, who presided, explained how knowledge of this recently discovered vitamin, which is remarkable for containing cobalt and for its potency in minute doses, had developed through two distinct channels. First, it had long been recognized that human pernicious anaemia could be cured by the administration of liver extracts. The active principle had been described by Castle as the "extrinsic" factor; in the absence of therapy it could not be absorbed in adequate amounts from the intestinal contents when the stomach wall failed to elaborate the "intrinsic" factor. Secondly, it had been noticed by workers interested in promoting rapid growth in farm animals, particularly poultry, that diets of entirely vegetable origin were unsatisfactory. The presence of an "animal protein factor" had been demonstrated, and its distribution studied in various foodstuffs of animal origin. Eventually it was realized that the human "anti-anaemic" factor could be identified with the "animal protein factor," and that the substance concerned could be classed as a water-soluble vitamin.

In spite of intense research our knowledge of vitamin B_{12} was still incomplete, particularly about its chemistry, the mechanism by which its absorption is assisted by the unidentified "intrinsic" factor, and its method of action in the tissues. The important interrelationship with folic acid had attracted much attention: while folic acid could cause a temporary improvement in the blood picture in pernicious anaemia it could not replace vitamin B_{12} in protecting the nervous system. Many other interrelationships, such as that involving folic acid, ascorbic acid, and tyrosine, required further investigation.

Isolation and Chemistry

Dr. E. LESTER SMITH described how vitamin B_{12} was first isolated from liver extracts by processes depending mainly on adsorption on charcoal followed by elution and chromatography on alumina. The numerous intricate operations had been facilitated when it was realized that the vitamin was highly coloured, and that its position on the adsorption column could be clearly observed as a bright pink region. Before the importance of this clue was realized progress towards the isolation of the crystalline vitamin had been retarded by the absence of a suitable animal test, which meant that all fractions had to be tested directly upon patients with pernicious anaemia.

Vitamin B_{12} was present in animal tissues, with liver and kidney as the richest sources, but absent from all plant tissues except small roots. It was synthesized by *Streptomyces griseus* and various other micro-organisms, and these had replaced liver as industrial sources. Presumably the accumulations of the vitamin in animal tissues were derived ultimately from micro-organisms.

Attempts to elucidate the chemical structure of vitamin B_{12} by hydrolysis had indicated the presence of a cyclized form of ribose and a benziminazole ring, and a small part of the molecule therefore appeared to resemble the vitamin riboflavin. The rest of the large molecule contained cobalt, a cyanide group, phosphoric acid, two 1-amino-2-propanol groups, and a large unresolved residue with the composition $C_{42}H_{55}N_9O_4$. Other active substances, differing slightly from vitamin B_{12}, had been detected in natural sources and prepared artificially. Numerous biological and microbiological tests were now available.

Therapeutic Value

Dr. C. C. UNGLEY discussed the value of vitamin B_{12} in the treatment of various forms of anaemia, and explained that it was only effective when the bone marrow was megaloblastic. Not all forms of megaloblastic anaemia, however, responded to therapy. Thus the anaemias of pregnancy and the puerperium, as observed in temperate climates, failed to respond to vitamin B_{12} but were corrected by folic acid. The so-called "tropical sprue" sometimes responded to vitamin B_{12}. Anaemia associated with cirrhosis of the liver was seldom megaloblastic, but, when it was, vitamin B_{12} might be effective. Anaemia after total gastrectomy had been corrected by folic acid, but not by vitamin B_{12}. Anaemia produced by a fish tapeworm had been cured either by vitamin B_{12} or by the expulsion of the worm; the parasite had been found to be rich in vitamin B_{12}, and presumably caused anaemia by absorbing supplies otherwise available to its host.

Dr. Ungley emphasized that, while vitamin B_{12} could correct not only the blood picture in pernicious anaemia but also the glossitis and nervous lesions, folic acid could only temporarily correct the blood picture. Doses of 1 μg. often produced definite improvement, but when patients had nervous lesions or suffered from intercurrent disease 100 μg. monthly should be allowed.

Dr. R. H. GIRDWOOD dealt with the complicated interrelationships between vitamin B_{12}, folic acid, and folinic acid both in the nutrition of micro-organisms and in the cure of anaemia. He concluded that both vitamin B_{12} and folic acid were necessary for normoblastic blood, and that folic acid was probably converted in the body to folinic acid. Other factors, such as ascorbic acid and the anti-anaemic factor of Wills, were also important, and the picture might be further complicated by the presence of inhibitory factors.

Dr. J. E. FORD described microbiological methods for the estimation of vitamin B_{12} based on the growth of *Euglena gracilis*, *Lactobacillus leichmannii*, and *Bact. coli*, and stressed the effect of the method chosen upon the comparative potencies of different sources of the vitamin.

Vitamin B_{12} and Other Growth Stimulants

Dr. W. F J. CUTHBERTSON gave an interesting account of the effect of supplements of vitamin B_{12} and certain antibiotics in promoting growth, mainly with reference to poultry. Widely different results had been obtained in different laboratories according to the diet given and to the condition of the poultry house. Poor growth was usually obtained when an exclusively vegetable diet was given without supplements, and vitamin B_{12} and other substances associated with it in its bacterial sources might then have dramatic effects in improving growth. When diets containing fish meal, however, or some other source of animal protein were supplemented by further supplies of vitamin B_{12}, or of an antibiotic such as "aureomycin," the findings of different workers might be very inconsistent. Thus with the same basal diet supplements of an antibiotic improved the growth of chicks in one locality but not in another. The cause of these disparities was presumably to be found in differences in the bacterial flora of the poultry houses. According to the nature of the bacteria they might either assist the chicks by synthesizing vitamin B_{12} and yielding it up on digestion in the alimentary tract or merely compete with the chick by absorbing such supplies of vitamin as were available in the food.

Miss M. E. COATES supported this view. Of two poultry houses in the same institute, one was new, while the other had been used for several years. Chicks grew equally well in the new house with or without antibiotics, but in the old house supplements of antibiotics caused a considerable increase in the growth rate. The restriction of hens to a diet deficient in vitamin B_{12} greatly reduced the hatchability of their eggs.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Homes for Incurable Children

SIR,—The Invalid Children's Aid Association is occasionally confronted with a small but very urgent need affecting a special class of child. Every doctor and midwife will have had experience of cases of babies with meningoceles who are paralysed and incurable, of babies with hydrocephalus at birth, with multiple congenital deformities, absence of limbs, osteogenesis imperfecta, and other rarer conditions. These babies are sometimes so deformed and so difficult to manage that they need special care, which they may not be able to get in their own homes or in ordinary nurseries.

This association would never wish to encourage parents to evade their proper responsibilities for their children, whether normal or abnormal, and many babies of the kind mentioned can be, and are, dealt with in their own homes. Our social workers are sometimes able to help parents and to put them in touch with available community services. But humanity and common sense sometimes dictate that other arrangements must be made for these babies if home accommodation is unsuitable, if there are older children who are still needing a good deal of care from the mother, or if the parents by temperament and character are unable to face the anxiety and heavy responsibilities entailed. At present, parents, almoners, children's officers, and others are sometimes faced with an emergency which leads to a frantic search for accommodation, and often the resulting arrangement is wholly unsatisfactory and inflicts considerable hardship.

Our association knows that, legally, public authorities should provide accommodation for children of this kind, but all too often the bed for the long-term case is just not there. We now propose to start and maintain a register of hospitals, nursing-homes, and suitably qualified private persons who are prepared to take on an especially difficult baby. Particulars of accommodation offered should be sent to the General Secretary, I.C.A.A., 4, Palace Gate, London, W.8. The number of cases involved is small, so that even a short list of suitable homes would be a real blessing in desperate need.—We are, etc.,

A. WHITE FRANKLIN,
Chairman, Executive Committee.
LETITIA FAIRFIELD,
Chairman, Homes Administration Committee.
G. RATTENBURY,
General Secretary.

Invalid Children's Aid Association,
London, W.8.

Death on the Roads

SIR,—During the last few years, acting as police surgeon, I have examined over 200 motor-car drivers arrested and brought to various police stations in the West End of London charged with being "under the influence."

Urine or blood tests are not usually employed. If the accused states that he has had no alcohol at all, a blood test for alcohol is asked for. In every case so far this request has been refused. Metropolitan magistrates have told me that they are not greatly impressed on being told that the blood contains a certain percentage of alcohol. They prefer to base their decision on the evidence of the police officers and surgeon. These magistrates have great experience, and they ought to know. The principal of a very well known London pathological laboratory tells me that these tests present certain technical difficulties, and that, as he is called upon only very seldom to perform them, he would prefer not to have that responsibility. If such tests are to be employed regularly it seems that it would be well to have each sample analysed at more than one laboratory.

The fate of the 200-odd cases examined may be of some interest. The following figures are approximate, but fairly accurate:

40% of them were dismissed by me. Half an hour or more elapses between the time of arrest and the time of examination. Arrest has a sobering effect. All these dismissed cases showed evidence of having had a considerable amount of alcohol, with the exception of three, all of whom were diabetics suffering from overdosage of insulin. This is the only condition I have come across which simulates drunkenness closely. Of the 60% certified by me about one-third plead guilty, of the remainder about one half elect to be tried by the magistrate; the others ask for trial by jury at the County of London sessions.

The magistrates find about 75% guilty. The court of sessions finds about 75% not guilty.

Even when the accused wins his case at sessions it is expensive; when he loses, it is very expensive, and the penalty is severe. Even so the gamble is well worth while. This 75% acquittal is a curious phenomenon. Cases which appear to be guilty beyond any possible doubt are frequently thrown out by the jury. It may be that the reason for this is to be found in the wording of the charge: "Being so much under the influence of alcohol as to be incapable of having proper control of a motor vehicle." Many cases are arrested as they are about to start their cars; others are able to show that they have in fact driven their cars some distance without mishap. In the first case there is no absolute proof that they were incapable; in the second it would seem that they were capable. Magistrates recognize the flaw in this sort of reasoning: juries apparently do not.

I have no legal training, and my opinion is of little value; but I believe that there would be more convictions and justice would be better served if the charge were amended to something like this: "Being in charge of a motor vehicle while so much under the influence of alcohol as to have one or more faculties noticeably deranged thereby."—I am, etc.,

London, W.9. JAMES GOSSIP.

Anticoagulants in Leukaemia

SIR,—Sir Lionel Whitby in Part II of his Refresher Course on leukaemia (December 29, 1951, p. 1573) has painted a picture of this disease which is easy to see and understand, and for which I am grateful.

In the treatment of chronic leukaemia there is, I suggest, one omission. He does not mention the use of anticoagulants in those cases where the thrombotic manifestations are prominent. In two of the three cases of chronic leukaemia which have come under my care mesenteric thromboses occurred, in one case agonizing in the intensity of pain. These were completely relieved of thrombotic signs and symptoms by keeping the prothrombin level around 65% of normal by the use of dicoumarol.

Sir Lionel mentions the distressing symptom of priapism and the possibility of surgical treatment. One of my patients developed this symptom and was relieved by anticoagulant treatment. I thought these observations might be of use to others.—I am, etc.,

Leeds, 8. R. A. MURRAY SCOTT.

Naevi in Pregnancy

SIR,—The letter of Mr. John Stallworthy (December 1, p. 1341) referring to the occasional appearance and growth of naevi associated with pregnancy prompts me to record a case I saw a few years ago.

The patient, a married woman with one child, noticed shortly after parturition the appearance of a small red papule in front of and just above the tragus of the right ear. There had been neither naevus nor telangiectasis on this site before or during pregnancy. The papule, which gradually increased in size, was itchy and bled when scratched. A few months later similar but smaller papules appeared on the tip of the helix of the same ear. Over the next two and a half years further lesions made their appearance while those that had appeared originally continued to increase in size. The new lesions were situated behind the right ear and on the skin of the face in front of the tragus.

There were no other naevi on her body, but she stated that at the age of 9 a red mark, unrelated to trauma, had appeared on the skin of her face in front of the right ear. This area, which was approximately 1½ in. (3.7 cm.) long by ¼ in. (0.6 cm.) broad, was telangiectatic and was noticed at the time of the examination.

On examination it was seen that the tragus and upper part of the helix of the right ear had been replaced by tumour tissue, and there were two lesions on the skin of the face near the ear. A similar lesion was present over the mastoid area behind the ear. The growths were not large, had a port-wine colour, were firm but rather spongy in texture, and blanched on pressure. General examination revealed no abnormality and a blood picture was normal apart from a slight degree of hypochromic anaemia. The W.R. was negative. A biopsy report stated that the lesion was a simple tumour of either lymph or haemangiomatous type, or both, with a heavy chronic inflammatory type of perivascular exudate in which eosinophils were outstanding.

The patient was treated with *x*-ray therapy with considerable regression of the tumour, but because of my National Service duties I was unable to follow the case further.

Although there are few references in the literature to the spontaneous appearance or growth of naevi in association with pregnancy the condition has been described by Whitfield (*British Encyclopaedia of Medical Practice*, 1937, **5**, 149) under the title "Progressive Angiomas of Pregnancy." He records a case of his own and quotes Gans as having figured a section of one from the cheek of a girl two months pregnant. Along the same lines Enticknap (*British Medical Journal*, 1946, **2**, 51) recorded a fatal case of angioblastoma occurring in the breast of a woman three months pregnant, which he considered to have arisen from a pre-existing simple haemangioma.

I would like to thank my former chief, Dr. A. D. McLachlan, physician, Diseases of the Skin, Western Infirmary, Glasgow, for permission to record the above case.

—I am, etc.,

Glasgow. W. O. THOMSON.

Cough Fracture in Late Pregnancy

SIR,—Dr. N. Wynn-Williams in his article on cough fracture (December 22, 1951, p. 1494) refers to a paper by myself and others on this condition in late pregnancy (*British Medical Journal*, 1949, **1**, 135). We described four cases and were able to find six others in the literature. The notable feature was that, in all, the left lower ribs were involved. It was our opinion that this fracture was relatively common in late pregnancy, and probably largely unrecognized. Dr. Wynn-Williams suggests that this fracture and pregnancy are a "fortuitous association" and not a clinical entity.

In the last two years I have seen four more examples in pregnant women, all left sided and affecting the lower ribs. No special effort was made to find them, other than a casual request to one or two of the assistants in the antenatal clinic to keep a look-out. Two were discovered in this way. The third came to light after I had overheard a conversation between a doctor and his wife about a patient requesting a visit. The fourth came to me because of chest pain of two years' duration.

I agree with Dr. Wynn-Williams that cough fracture unassociated with tuberculosis is common enough, and have seen six other such patients in the last four years; however, in these there is no such clear-cut tendency for the left side to be affected as there seems to be in our series. We discussed some of the possible causes of this left-sided predominance in our paper. The fact that all cases so far reported have occurred in the last three months of pregnancy cannot easily be dismissed as due to chance.—I am, etc.,

Ipswich. J. W. PAULLEY.

Skin Resistance to Ultra-violet Light

SIR,—Dr. Klaus A. J. Järvinen, of Helsinki (December 8, 1951, p. 1377), has reported some interesting observations on the effect of systemic cortisone therapy on the reaction

of the skin to ultra-violet light. He has found that it doubles the minimal erythematous dose, and he also states that when the same patients were submitted to six minutes' exposure before, during, and after cortisone therapy the effect of cortisone was to promote pigmentation and, as one might therefore expect, to diminish the harmful erythematous and vesicular reaction.

From these simple and precise observations Dr. Järvinen draws the somewhat surprising conclusion that in this respect cortisone is not increasing the resistance of the skin to the injurious effect of ultra-violet light, but rather suppressing the normal protective mechanism by which this resistance is augmented and maintained. This can be true only if we regard erythema and vesiculation as a protective mechanism and pigmentation as an injurious effect. Since the opposite is a more prevalent teleological interpretation of the phenomena of photosensitivity, I would like to submit that his experiments indicate a true increase in the resistance of the skin to ultra-violet light as exemplified by the doubling of the minimal erythematous dose and that they also suggest a stimulation of the protective mechanism if we are entitled to regard pigmentation in this light.—I am, etc.,

Merck and Co., Ltd., Montreal. J. H. LAURIE, Medical Director.

Night Pain with Fractured Clavicle

SIR,—Within the last 10 weeks I have had two cases in children under 5 of fracture of the outer third of the clavicle. Clinically they have been misleading in that there is no deformity; there is practically no loss of function—the child has been able to dress and undress itself apparently without pain, including pushing the affected arm into a jersey, etc.; there is no apparent general disturbance. There has, however, been one feature common to both cases, and that is pain at night in bed. I suppose the anatomical structure maintains position while erect, but on lying down and turning over in bed pressure is brought on the fracture, or is it relaxation of muscles while asleep? Both cases were found on *x*-ray examination.

I wonder if any other people have found this pain-in-bed story connected with fracture of the outer third of the clavicle in young children.—I am, etc.,

Hadlow, Kent. J. B. MARSHALL.

Treatment of Anthisan Poisoning

SIR,—Your report of a further two cases of "anthisan" poisoning in children (December 22, 1951, p. 1530) prompts me to take out of their context some of the results of an investigation into the cerebral effects of histamine. This investigation, which will be published eventually, necessitated the administration of anthisan in toxic doses to a large number of animals. The findings were so uniform in all the species examined (mouse, rat, guinea-pig, and rabbit) as to favour the view that they might also apply to human beings, especially as the clinical features of anthisan poisoning are very similar in man and animals.

Anthisan is a central convulsant—i.e., the convulsions seen in poisoning are not a secondary effect of interference with respiration, as is sometimes suggested, but depend on a direct action of the drug upon nervous centres. The average convulsive dose is very near the average lethal dose, and the gravest view must therefore be taken of any case presenting convulsions. Death is the result of respiratory depression, which occurs after the animal has passed through the convulsive stage. With slow absorption of the drug the central nervous system shows successively depression, excitement and increased reflex activity, tonic-clonic convulsions, coma, and respiratory depression. These stages correspond to the severity of the intoxication, and all four stages are therefore only seen with fatal or near fatal doses. Anthisan may be classified with atropine as a "deliriant narcotic," and their similarity of action is not fortuitous.

Orthodox anticonvulsant drug therapy is likely to prove disastrous in anthisan poisoning. The administration of ether, chloroform, soluble barbitone, or "nembutal" to experimental animals, while leading to a prompt cessation of the convulsions, greatly diminishes the survival rate by hastening and deepening the stage of respiratory depression. It should be remembered that convulsions, unless of great severity and long duration, are not a life-threatening symptom in themselves. Their abolition is therefore not usually a legitimate therapeutic aim unless it is achieved by means which relieve rather than deepen the underlying intoxication of the central nervous system.

The effect of histamine on anthisan poisoning is markedly diphasic. In relatively small doses it has an important anticonvulsant and life-saving action, while in larger doses it increases mortality. With simultaneous administration the greatest life-saving effect is produced by an anthisan: histamine acid phosphate ratio (weight for weight) of 4:1 in the guinea-pig and 1:1 in the mouse, using average lethal doses of anthisan. To translate this finding into terms of human therapy is extremely difficult, not only because of species difference but also because poisoning in human cases is usually by mouth and the amount swallowed is rarely known. Moreover, animal experiments suggest that it is very difficult to dislodge anthisan from its central receptors, and histamine therapy becomes successively less effective as the interval between anthisan and histamine administration grows. In spite of this, a cautious trial of histamine in these desperate cases can be recommended, especially as absorption of anthisan is often still proceeding when they are first seen by a physician. If histamine is tried as an antidote, steps must be taken to protect the patient from the acute and severe hyperchlorhydria which will ensue.

Morphine occupies theoretically an ambivalent position in the treatment of anthisan poisoning. As a respiratory depressant it would seem to be contraindicated, as a histamine-releasing drug it might be an ideal therapeutic agent. Preliminary trials in mice have not yet given an unequivocal answer, but I think that a clinical trial of its efficacy as an antidote would be justifiable. Judging from animal experiments, it is certainly preferable as a sedative to barbiturates in these cases.

Adrenaline and atropine hasten death from anthisan poisoning in experimental animals.

On these imperfect data we may base the following scheme of treatment:

1. Wash out the stomach.
2. Treat the patient in a darkened room and avoid all unnecessary stimulation.
3. *Do not administer inhalation anaesthetics or barbiturates.*
4. If drug therapy seems desirable, try morphine or histamine, the latter in doses no greater than the amount (weight for weight of histamine acid phosphate) thought to have been absorbed by the patient.
5. Watch for respiratory depression, and give respiratory stimulants if it supervenes.
6. Take any supportive and eliminative measures which are not in conflict with the above.

An improved outlook in anthisan poisoning will result from the conscientious reporting of all cases with full notes on the treatment, even if unsuccessful. Meanwhile a certain number of lives may be saved by attention to these (largely negative) injunctions.

These observations probably apply to a greater or lesser extent to all antihistamine drugs. They are all central convulsants in toxic doses, and it is to be assumed that the mechanism of production of toxic manifestations is the same. I cannot conclude these remarks without making reference to the great help which I have received from Dr. Roy Maxwell, of May and Baker, Ltd., both in the supply of drugs and in the giving of expert advice.—I am, etc.,

Edinburgh. ERICH GEIRINGER.

Discovery of the Formol Gel Reaction

SIR,—I am very much indebted indeed to Colonel W. C. Spackman for his letter (October 13, p. 911) about the discovery of the formol gel reaction, as it provides a very good opportunity for me to give a short account of the history of this discovery in the light of real facts, and not as presented in some publications.

In September, 1920, while I was a medical student and assistant at the Diagnostic Laboratory of Dr. Gaté, of the Bacteriological Institute of Lyons (France), there was a violent explosion that destroyed part of the Institute, including the refrigerator in which I used to keep the mixture of positive and the mixture of negative

serums of the previous week's Wassermann tests. Being at that time responsible for these tests and wondering where to keep the serum-controls each time used, I thought of adding to them a few drops of formol.

When I next wanted to use these serum-controls I observed that the positive mixture had jellified and was stuck to the bottom of the test-tube, while the negative mixture remained fluid, with no change whatsoever. This phenomenon seemed strange to me, and made me wonder whether, if repeated, it could not be used as a specific reaction for the diagnosis of syphilis. I tested immediately with formol some serum specimens, syphilitic or not, that I had available, and next day I observed that the former became jellified while the latter remained unchanged. I communicated this to Dr. Gaté, who during the succeeding days sent me from the Antiquaille Hospital of Venereal Diseases, in which he was assistant, a great number of syphilitic blood specimens for testing them comparatively with formol and at the same time by the Wassermann reaction.

The experiment was simple: To 1 ml. serum in an ordinary test-tube I added two drops of formol. Within 24–30 hours most of these sera jellified, and the results corresponded with Wassermann results in 85% of cases. The findings of this research were presented to the Société de Biologie at its meeting of November 15, 1920, and the relevant communication, entitled "Une nouvelle réaction des sérums syphilitiques: Formol-Gélification," appeared in the *Comptes rendus de la Société de Biologie*, 1920, **83**, 1432.

The reaction being easy to carry out, there followed a great number of publications, from which, as well as from our own, it was proved that the formol gel test is not a specific syphilis reaction, but occurs in various diseases and is due to some abnormality of one or more constituents of the blood serum. The reaction was naturally tested both by us and many other research workers in connexion with various diseases. It was also tested, for the first time, in kala-azar by Colonel Spackman,[1] who observed that its occurrence in that disease was very quick, and that besides getting jellified the serum also became turbid. He therefore suggested that the formol gel reaction might also be strongly positive in trypanosomiasis.

A month later[2] it was reported that Napier "has *discovered* a test which promises to be of great value in the diagnosis of kala-azar . . ." and that "the test is a *modification* of that described by Gaté and Papacostas, who found that the serum of syphilitic patients becomes jellified in 24 to 30 hours when to 1 ml. clear serum two drops of commercial formalin solution are added. When this test is applied to the serum of kala-azar patients an immediate white opacity develops and the serum jellifies within half an hour."

There followed almost immediately[3] a communication by Fox and Mackie, stating that they were studying the Gaté-Papacostas reaction in kala-azar from July 21, 1921, and reporting the results of their research.

The findings of Napier's study were published by him seven months later.[4] In addition to kala-azar, he reports a number of cases of other diseases in which he tested the reaction. In his study he states that in carrying out the test he used the technique described by Gaté[4] and Papacostas. Owing, however, to the quickness with which kala-azar patients' sera become jellified and turbid, he deemed it advisable to redesignate the formol gel test of Gaté and Papacostas as the "aldehyde test" or "Napier test,"[5] and has since used this reference for the formol gel reaction in all his papers, as well as in his book *The Principles and Practice of Tropical Medicine* (1946).

Let us now see how far this redesignation of the reaction can be justified.

As is known, when speaking of any chemical reaction whatsoever we mean "the action set up by one substance on another" (*Concise Oxford Dictionary*). Therefore for any chemical reaction two things are necessary—the reagent and the substance on which it reacts. In the case of the formol gel reaction, the two interacting substances are formol and blood serum.

Both Spackman and Napier used the same reagent as we did—i.e., formol—and on the same substance—the serum. In addition, they used the same technique—namely, 1 ml. serum, two drops of formol, and the ordinary laboratory temperature. The test, therefore, used both by Spackman and Napier is exactly the same as we first described and is as now universally used. And if in some diseases the reaction somewhat varies in regard to time and turbidity, this, we believe, can by no means justify a special redesignation of the reaction in each particular case. Furthermore, according to Napier the two specific features of the formol gel reaction whereby he justifies its redesignation to "Napier test" are not encountered exclusively in kala-azar cases. Numerous writers have noted that the quickness of reaction and turbidity do not constitute a rule in kala-azar, nor do they represent exclusive characteristics of this disease. In this connexion we would refer, among others, to the relevant study of Froilano de Mello and Baretto,[6] who observed the same opalescence in sera of malaria patients, lepers, and dysenteric and syphilitic persons. Napier himself,[4] in his first study, reports kala-azar cases in which solidification occurred without complete opacity. I also, having studied kala-azar reactions for years in Greece, observed a great number of cases where reaction developed many hours later, and in others there was no turbidity. I sometimes noted these phenomena in the same patient at different times.

We now know some more morbid conditions in which the formol gel test appears as in kala-azar. This especially applies to Kahler disease (multiple myeloma), which was thoroughly studied by Bing,[8] E. Delbarre,[7] and others. In that disease jellification of serum occurs within a few minutes, and is followed by an intensive turbidity. According to Delbarre, in the above disease formol gel reaction is a fundamental symptom. But neither Bing nor Delbarre ever thought of changing the name of the reaction.

In one of our later studies, in 1922,[9] on the formol gel reaction in various diseases we drew the conclusion that "the reaction is not specific for syphilis, and that it seems to act as a control of unknown humoral changes, possibly caused by general chronic morbid conditions," and in another communication[9] we stated: "Like so many other humoral reactions or blood tests, such as eosinophilia, which no one claims to be specific for a certain disease, but the theoretical and practical diagnostic value of which in many diseases no one questions, the formol gel reaction—a new blood serum test—though not specific for one disease, maintains its value for many morbid conditions. . . ."

At present, from numerous researches made by various workers, it appears that the formol gel reaction is due to the disequilibrium of serum proteins and particularly to the reversal of the albumin-globulin ratio. According to many writers, this is due to an increase in the globulin fraction, but several others think that, for its occurrence, some other secondary, but necessary, unknown factors are required.

Regarding the use of formol gel reaction in surra (trypanosome disease of camels), to which Colonel Spackman refers in his letter, priority in its application pertains to the French Plantureux,[10] who published his relevant study eight months before Colonel Spackman's publication.[11]

I have thought it necessary to set forth the foregoing details in order to put an end, once for all, to the confusion appearing in some publications, especially English and American, about the history and origin of formol gel reaction.

I wish to thank Colonel Spackman again for the opportunity he offered me by his communication, as well as the Editor of the *British Medical Journal* for his courtesy in publishing this long letter.—I am, etc.,

School of Hygiene, Athens.

GEORGE PAPACOSTAS,
Professor of Public Health and Social Medicine

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5 *Bull. Soc. Path. exot.*, 1926, **19**, 127.
6 *Acta med. scand.*, 1937, **91**, 336; 1940, **103**, 547.
7 *Congrès Français de Médecine, 18e session, Genève*, 1949, Paris, Masson, 1951, p. 145.
8 *C.R. Soc. Biol., Paris*, 1922, **87**, 543.
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Gastric Carcinoma and Acute Perforation

SIR,—I read with great interest the article on acute perforation of gastric carcinoma by Mr. T. L. Kennedy (December 22, 1951, p. 1489), and it recalled to my mind a case which I operated upon about two years ago which showed some unusual features.

On October 28 a man aged 41 was admitted with a very severe epigastric pain of three hours' duration. There was a five-year history of epigastric pain which came on about two hours after meals and showed periods of remissions and exacerbations. In the last month before admission the pain had become very severe, but it was still related to meals. His appetite was good except in the week previous to admission, when he had taken very little

solid food because he was afraid to eat. When he was admitted he had typical symptoms and signs of a perforation, and from the history it was reasonable to assume it to be a perforated duodenal ulcer.

At operation there was a perforation in the anterior wall of either the first part of the duodenum or of the pyloric antrum of the stomach. As there was so much oedema it was difficult to say with certainty the exact site of the perforation. The perforation was dealt with and the patient made a rapid recovery. On the 14th day he was transferred to a medical ward, as was the usual practice in that hospital.

A fractional test meal on November 29 showed a normal free acid curve, but a trace of blood was found during the second and third hour. A chest radiograph taken about the same time was normal. On December 9 a barium meal showed a suspicious persistent filling defect in the pyloric antrum. Three days afterwards a gastroscope was passed, but for no obvious reason would not pass beyond the cardiac sphincter.

It was noted on December 16 that his appetite was very good, but on December 19 he developed a slight pyrexia which persisted. His general condition from now on began to deteriorate. His haemoglobin was found to be only 53%, but despite repeated blood transfusions there was little improvement in the anaemia. It was thought to be an aplastic type, possibly due to secondary growths in the bone marrow. Blood culture had been found to be negative. On December 20 a chest radiograph revealed an opacity in the left upper zone, and on January 6 early ascites was noted and this became worse in the next few days. His general condition deteriorated and he died on January 28—exactly three months after the operation.

At necropsy he was found to have a carcinoma of the pyloric antrum, with an unusual pattern of secondary growths in the lungs, left suprarenal, and in several ribs.

The interesting features about this case were the history, suggestive of a perforated duodenal ulcer; the fractional test meal —no achlorhydria; that his appetite was good, even up to six weeks after operation; and that the condition deteriorated so rapidly after operation that one would infer that secondaries were present at the time of the perforation, and a gastrectomy would not have prolonged life. This finding agrees well with the general poor ultimate prognosis in these cases.

—I am, etc.,

Swansea. W. O. WILLIAMS.

POINTS FROM LETTERS

Inflation of Lungs During Bronchoscopy

Dr. R. A. C. HERRON (Zürich) writes: I was most interested to read the article by Dr. R. Bryce-Smith (December 22, 1951, p. 1517) on inflation of the lungs during bronchoscopy. I was also gratified that this method should receive the wide publicity it deserves, as I have been using it for three years and know the obvious advantages, especially in safety for the patient (*Anaesthesia*, 1950, **5**, 40).

Invite Russian Doctors

Dr. JOHN PEMBERTON (Sheffield) writes: I would like to support Dr. R. L. Kitching's suggestion (December 1, 1951, p. 1331) that the British Medical Association should invite a group of Russian doctors to this country. In addition to leading to a valuable exchange of medical knowledge and experience, such a visit might contribute a little towards a better understanding between our two countries, especially if our Russian colleagues were willing to stay with us in our homes.

Tissue Reactions to Protein Sensitization

Dr. J. T. SHIRLAW (Wigan) writes: "The eosinophil cell is worthy of greater attention," says Professor J. R. Squire in his lecture (January 5, p. 1). So far, the following facts have been established: Allergy is accompanied by an eosinophilia; the administration of cortisone brings about an eosinopenia together with a dramatic improvement in allergic diseases; cortisone lessens cell growth activity. Surely these are points of great significance. I do not agree that the "eosinophil may be regarded as being concerned with 'mopping up' the products of tissue damage"; the eosinophil only appears on the scene when the mopping-up process has been finished by other leucocytes and should therefore be regarded more as a repair cell. . . .

Correction

In the paper on "Tuberculous Meningitis," by Dr. S. Russell Jamieson (January 12, p. 83), in Case 29 (p. 84, column 2) the dosage of vitamin B_{12} employed was given as 10 mg. This was a thousand times too high, and should read 10 μg.

Obituary

H. S. RAPER, C.B.E., D.Sc., M.B., F.R.C.P., F.R.S.

The death of Professor H. S. Raper on December 12 was recorded in the *Journal* of December 22 (p. 1527). We are indebted to Professor A. Wormall for the following appreciation.

The passing of Henry Stanley Raper removes from the ranks of British biochemists one of its most distinguished and revered leaders. His approach to medicine was basically scientific, for he was a member of that small but remarkable group of chemists who qualified in Leeds in the early 1900's and subsequently branched out and helped to develop the new chemical offspring, biochemistry. This group included Dakin, Dudley, Hartley, Raistrick, and Raper, and all have made contributions which will for ever keep their own names, and indirectly the name of their chemistry mentor, the late Professor J. B. Cohen, permanently recorded in the annals of biochemistry.

Raper's main interest was undoubtedly in medical science, but he was above all a magnificent chemist. His whole approach to physiology and medicine was through chemistry and biochemistry, and, although for the greater part of his career he was professor of physiology at Leeds or Manchester or Dean of the Faculty of Medicine at Manchester, he never lost his keen interest in all branches of biochemistry. His ability to keep up to date, and indeed to anticipate many new developments, made him the ideal adviser-in-chief. Chemists, biochemists, physiologists, bacteriologists, pathologists, and clinicians came to him with their problems, and rarely, if ever, did they go away without at least one and usually several valuable constructive ideas.

His biochemical interests were wide. With Leathes he wrote an excellent classical monograph on fats, and during the 1914–18 war he made valuable contributions in the field of chemical warfare defence. He was one of the first in this country to use (in 1936) deuterium in the study of the absorption and metabolism of fats, and in recent years, in collaboration with Harper, he made important advances in our knowledge of the hormone pancreozymin. It is probable, however, that he will best be remembered in biochemistry for his classical work on tyrosinase, an oxidizing enzyme responsible for producing much of the dark-brown and black pigmentation of many animals. It is to Raper and his colleagues that we owe our knowledge of the precise chemical changes involved in the enzymic conversion of the amino-acid tyrosine into the red pigment hallachrome which is the precursor of melanin.

His happiest working hours were spent in his laboratory. "How delightful it is," he wrote to me early in January, 1945, "to be able to use one's hands and do a few experiments. But alas, term begins on Tuesday with its lectures, committees, interviews, and what not, so it will only be in odd hours that I can escape to the laboratory bench." Many biochemists will regret that with his almost unrivalled skill as a biochemist he was given so little opportunity to develop the work he loved, but we may be happy in the knowledge of the major contribution he made in the wider field of medical education and in the organization of medical research. His friends, and they were truly legion, will treasure the memory of "a verray parfit gentil knight," in stature and in deed.

R. FOSTER KENNEDY, M.D., F.R.S.ED.

Dr. Robert Foster Kennedy, professor of neurology at Cornell University Medical College, and formerly president of the American Neurological Society, died in New York on January 7, aged 67.

Robert Foster Kennedy was born in Belfast. His grandfather was Professor R. F. Dill, and one of his cousins was the late Field-Marshal Sir John Dill. He

studied medicine at Queen's University, Belfast, graduating in 1906. Shortly afterwards he came to London as resident medical officer at the National Hospital for Nervous Diseases, Queen Square. In 1910, the year he was elected a Fellow of the Royal Society of Edinburgh, he accepted a post in the New York Neurological Institute. From then his reputation grew steadily, not only as a neurologist, but as a scholar, wit, and outstandingly good orator.

During the first world war he served with the British and French Armies and made a special study of shell-shock. He was mentioned in dispatches and created a Chevalier of the Legion of Honour. He received many honours during the course of his distinguished career: last year Queen's University conferred on him the honorary degree of D.Sc.

Dr. Macdonald Critchley writes: Dr. Foster Kennedy was "in the house" at the National Hospital, Queen Square, at the same time as the late Kinnier Wilson. This apprenticeship brought him in touch with such masters as Bastian, Horsley, Ferrier, Gowers, and Hughlings Jackson. When Foster Kennedy elected to leave this country and settle in New York he took with him the tradition of clinical brilliance which, added to his own great powers, rapidly and surely achieved success.

It was not long before Foster Kennedy acquired a considerable consulting practice, as well as a reputation as a teacher and a clinician of outstanding merit. Slowly his distinction throughout North America increased, until in the last few years he found himself the leading exponent of medical organic neurology in the United States. His numerous contributions included the "Foster Kennedy syndrome" of subfrontal tumours and considerations upon aphasia, especially loss of artistic ability after local brain disease. He was interested in the difficult problem of the relationship between the loss of speech and the level of general intelligence. Latterly his attention was turned to the neurological complications of spinal anaesthesia and to the nervous manifestations of allergy.

But if Foster Kennedy's place as a neurologist is well assured, he will surely be best remembered as a generous, cultured, courteous, and kindly friend. His patients, pupils, and colleagues held him in such esteem as is rarely found nowadays. He kept in close touch with neurologists in Europe, and his friends in Great Britain and his native Ulster were very numerous indeed. Mr. St. John Ervine has recently dedicated his latest volume to Dr. and Mrs. Foster Kennedy.

It is a commonplace observation—though not often expressed openly—that doctors make the best diplomats: certainly Great Britain never had a better ambassador in the New World than Foster Kennedy.

For the last year or two Foster Kennedy had borne with supreme patience the vicissitudes of an insidious but fluctuating illness which ironically enough entailed alarming neurological manifestations. Throughout this illness the patient's charm and courage were inextinguishable. Neurologists throughout the world—and particularly in this country—will mourn the passing of a great colleague and a great man.

F. J. H. writes: American medicine has lost a unique and distinguished personality by the death of Dr. Foster Kennedy. More than 40 years of practice in the United States did nothing to change his essentially British characteristics. He loved the country of his birth and its way of life, and he loved the sea. To pass from the hectic din of New York into the quiet garden of his charming old-world house on the East River was an unforgettable experience. Here he loved to sit and talk in his soft and gentle voice; for he was an entrancing conversationalist and a truly cultured man. His nature was kind and lovable, but he could yet display the fire of the reformer and determination of the pioneer, fiercely attacking what he considered wrong or specious. Foster Kennedy understood well the meaning of real friendship, and his passing is a deep personal loss to those who were privileged to know him.

DALLAS B. PHEMISTER, M.D., F.A.C.S., F.R.C.S. (Hon.)

We announce with regret the death of Professor Dallas B. Phemister, of Chicago. He was 69 years of age. We are indebted to Sir Harry Platt for the following appreciation:

Phemister graduated in medicine from the old Rush Medical College in 1904, and after holding a number of resident posts began to prepare himself for his chosen career in academic and practical surgery by a training in physiological research. To this end he came to England and worked for a time with Starling at University College. His ambition was early realized in his appointment, soon after the first world war, to the full-time chair of surgery in the University of Chicago, with charge of the surgical division of the new Billings Memorial Hospital. Phemister soon became a force in American surgery, and, by the example of his outstanding integrity and single-minded devotion to the pursuit of truth, he set a standard both for himself and for his pupils which was always a challenge to the notion of material success as the hallmark of surgical leadership. Although he remained to the end a general surgeon—whatever that term may convey—Phemister's chief interests lay in the field of orthopaedics—bone growth, bone grafting, the arrest of longitudinal growth in young bones, the healing of fractures, and tumours of bone. His notable contributions to these subjects were always founded on a combination of experimental and clinical observations. He was elected a member of the American Orthopaedic Association in 1923, and many of his earlier papers were read before meetings of this body. He also played an influential part in the affairs of the American College of Surgeons, both as Regent and as Chairman of the Committee on Postgraduate Training. In 1949 he occupied the distinguished office of President, and in his presidential address expounded the virtues of the American version of the full-time professorial system in university departments of surgery, whereby the professor and his senior staff were remunerated by a composite salary to cover the three activities of teaching and research, the treatment of public patients, and the treatment of private patients within the university hospital.

On first acquaintance Phemister gave the impression of austerity, but behind a quiet and dignified exterior was a man capable of warm friendships. He was also in the best sense a "good European," and he valued highly the distinctions which came to him outside his own country—the Honorary Fellowship of the Royal College of Surgeons of England (1947), and the Vice-Presidency of the International Society of Surgery at the Congress in Paris in September, 1951, during which he received the Legion of Honour. As Emeritus Professor of Surgery in the University of Chicago he had just begun to look forward to further years of fruitful surgical research. During the meeting in Paris, his many British and Continental friends perceived no signs of decline in his mental and physical vigour. His death following an operation for appendicitis has removed from the world of surgery a man with unique personal and intellectual qualities who still had a message to deliver.

HENRI HARTMANN, M.D., F.R.C.S. (Hon.)

Dr. Henri Hartmann, who was appointed professor of clinical surgery in the University of Paris in 1909, died in Paris on January 2, aged 91. We are indebted to Mr. V. Zachary Cope for the following appreciation.

Probably no French surgeon has been, in his day, better known or more widely respected than Henri Hartmann, who as long ago as 1913 was thought worthy to be elected an Honorary Fellow of the Royal College of Surgeons. Anatomists still describe the "pouch" which bears his name, and surgeons still, in selected cases, practise the operation he devised for some cases of carcinoma of the rectum.

Henri Hartmann was born in Paris in 1860. He was a successful medical student, and gained the Prix d'Argenteuil in 1887. He became successively hospital surgeon, *agrégé*, and professor at the faculty of medicine, and in 1918 was elected a member of the Academy of Medicine, of which he became president in 1936. In 1929 he had the distinction of presiding at the meeting of the International Society of Surgery held in Warsaw. In 1932 his friends and pupils presented him with a jubilee book to celebrate his 50 years of professional life.

Hartmann succeeded in 1909 to the chair of surgery at the Hôtel Dieu, where he performed about a thousand operations yearly for 20 years or more. He kept personal notes of all his cases, and had a wealth of experience that he drew upon in his many published works. He was a general surgeon in the best sense of the word. He wrote on tumours of the breast and on the treatment of war wounds, but his main work was within the abdomen. He wrote books on the surgery of the stomach, of the biliary passages, and of cancer in general; he also published a good book on operative gynaecology which was translated into English, and was for several years editor of *Gynécologie et Obstétrique*. He was one of the founders of the French League against cancer, and for his public work and distinction he was made a Grand Officer of the Legion of Honour.

Hartmann's clinic in Paris drew men from all parts of the world, and English surgeons regarded him as a man of outstanding surgical worth. The present generation furnishes few, if any, examples of such all-round surgical proficiency. In spite of the great activity of his life he reached a ripe old age.

The death occurred at St. Andrews on December 29 of Dr. JOSHUA FERGUSON in his 82nd year. He was the son of the Rev. Dr. Fergus Ferguson, a leading minister in Glasgow in his day. From Glasgow High School Joshua Ferguson went on to Glasgow University. He was a brilliant scholar, being prosector in anatomy from 1892 to 1894, taking his M.B., C.M. degrees with honours in 1895, and winning the coveted Brunton Memorial Prize awarded to the most distinguished medical graduate of the year. This reputation remained with him in after-years, and many of his fellow graduates continued to speak of him as "The Master." After a period in the Glasgow Western Infirmary he came to Paisley as an assistant to another notable doctor, the late Dr. Donald Fraser, and later he started on his own account. He practised in the town for over 40 years and was soon recognized as the leading physician in Paisley and district. Among his appointments were those of visiting physician to the Royal Alexandra Infirmary and the Royal Victoria Eye Infirmary, medical adviser to the firm of J. & B. Coats Limited, physician to the Coats Sanatorium, and medical referee in Renfrewshire under the Workmen's Compensation Acts. He was a Fellow of the Royal Faculty of Physicians and Surgeons in Glasgow and for a term he was president of the Royal Medico-Chirurgical Society of Glasgow. Apart from the practice of medicine he had many other interests. A man of wide culture and learning, he had studied and absorbed all that was best in Greek, Latin, and English literature. As evidence of the extent and quality of his interests he was a president of the Paisley Philosophical Institution and for a term president of the Scottish Photographic Salon. Dr. Ferguson was a brilliant public speaker, his speeches being models of perfect phrasing and brightened by flashes of wit. He was a devoted churchman and for many years an elder in Paisley Abbey. It is not possible in a short appreciation to give a true picture of his qualities. One of his younger colleagues spoke of him as the ablest and most versatile man he had known intimately. His many patients remember him above all as the perfect doctor: he had remained a student all his life and kept himself in touch with all modern developments in the practice and art of medicine, so that he could proffer all that was best for their benefit. He had a way of inspiring confidence both in young and old, and his presence at a bedside was in itself a comfort and a cure. Dr. Ferguson retired in 1939 to St. Andrews. He is survived by his widow, a sister of the late Viscount Horne, who was Chancellor of the Exchequer after the first world war.—T. H.

Dr. W. H. MILLER, formerly senior surgeon at Bedford General Hospital, died suddenly at home on December 31, 1951, aged 70. Born in Newcastle-upon-Tyne, the eldest of a large family, William Henry Miller went with his parents to Canada, from whence he returned in 1893. He was educated at the William Ellis School in London, and went on from there to Guy's Hospital, where he won the Durham and Hilton Exhibitions. He qualified in 1906, graduated M.B., B.S. with honours in 1907, and proceeded M.D. with first-class honours and gold medal in gynaecology in 1911, the same year in which he became a Fellow of the Royal College of Surgeons. After acting as house-surgeon at Guy's Hospital, he became surgical registrar at the Samaritan Hospital. He went into practice first in Enfield, and then joined the late Dr. Hartley in Bedford. In the 1914–18 war he served as a surgical specialist in the R.A.M.C. Returning to Bedford after the war, he took over Dr. Hartley's practice, and eventually became the head of a large partnership. Always interested in surgery, he was appointed assistant surgeon to the Bedford County Hospital in 1924, and in 1932 he succeeded Mr. W. G. Nash as senior surgeon and chairman of the medical staff committee. When the National Health Service came into being in 1948 he was appointed consultant, and continued to do surgical work at the hospital until March, 1951. During this time many changes took place in the work of the hospital, and it was largely due to his inspiration and untiring enthusiasm that the hospital was brought so thoroughly up to date before the Ministry took over. At first interested in gynaecology, he became later expert in gastric surgery, which he raised to a very high standard in Bedford. He was particularly keen on giving his registrars and house-men a really practical training, and many will be grateful to him for his help and encouragement. This, too, can be said for his partners in general practice, where again he led the way by a very high standard and example. He was a most valuable member of the Bedford Group Hospital Management Committee, on which he served from its inception till the time of his death. He acted, too, as medical adviser to the Bedfordshire Hospital Services Association, where his sound judgment was greatly prized. During the second world war he was chairman of the local medical war committee. His life was saddened by the loss of his eldest son in 1940. He leaves a widow, a son, and a daughter.

A colleague writes: It is sad to contemplate practice in Bedford without the help of our great friend Dr. W. H. Miller. He was a strong man, and many of us learned to rely on his judgment not only in medical matters but in other directions as well. His opinions were decided, and never indefinite: they were mellowed by a very real humanity. Many of his friends and patients were delighted by the twinkle in his eye and by his charm and friendliness.

He was a man who never spared himself, and he inspired others to work with him. One felt that he really cared for the welfare of those for whom and with whom he worked, and he would take endless trouble to promote their interest both by sound advice and by practical help. He was a great fighter for things he thought right, and we all admired him for it. I know I express the feelings of all his old colleagues, patients, and friends when I say that his sudden death leaves a sense of great personal loss and that he will be sadly missed by everyone who knew him in Bedford.

Medico-Legal

EXPLOSION DURING ANAESTHETIC

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

On October 23, 1951, Mrs. Bessie Freeman, aged 55, who had been admitted to the Royal National Throat, Nose, and Ear Hospital, London, on the previous day for radical mastoidectomy on the right side, was found fit for operation, and about an hour and a half before the scheduled time was given premedication with "omnopon" ¼ gr. (22 mg.) and scopolamine 1/150 gr. (0.43 mg.). This was followed by "flaxedil" and thiopentone, and oxygen was then administered in the anaesthetic room. The anaesthetist was controlling the valve of the oxygen cylinder on the anaesthetic trolley and giving her the oxygen through an insulated rubber breathing-bag and facepiece, when there was an explosion. It appeared to be in the face-piece where he was holding it on the patient's face. He was thrown to the floor, and there was a fire on the trolley.

The patient was brought out of the room and aided respiration was maintained and an intratracheal tube passed. Her eyelashes were singed, her eyelids were bruised, and her nose was bleeding. In the theatre some blood was removed from her nose and pharynx, and bruising of the palate and post-pharyngeal wall was noticeable, but there was no active bleeding. As her pulse was good, and as her general condition seemed to warrant it, the surgeon decided to perform the operation. One hour and ten minutes after the explosion the patient collapsed. The operation had proceeded normally until then and was nearly finished. In spite of continuous restorative procedure the patient died in the ward about an hour and ten minutes later.

At the inquest, held before the North London coroner, the explosion was ascribed to static electricity, possibly sparking from the breathing-bag, where it might be generated by the movement of the bag itself, or from the movement of the anaesthetic tube against the patient's blanket. The bag was burst in the explosion. The anaesthetist's shoes were satisfactory and within the limits prescribed by the Ministry of Health, but atmospheric conditions in the anaesthetic room had been very favourable for the generation of static electricity. There was, however, no conclusive evidence of the cause of the explosion.

At necropsy the pathologist, Dr. F. E. Camps, found bruising of both upper and lower eyelids. There was bruising of the gullet right down to the stomach, of the larynx, and at the back of the throat. The force of the explosion was such that the stomach had been over-distended and had burst into the abdominal cavity. There was bruising round the heart and of the intestines, and rupture of the spleen and of the right lobe of the liver. There were some areas of bruising in the lungs, but the main force of the explosion had gone into the stomach. He said that nothing could have been done to save the patient's life after the explosion, and an exploratory operation of the abdomen would only have hastened her death. In spite of the extent of her injuries she might well have shown no symptoms except for a drop in blood pressure, and before the operation she had been suffering from high blood pressure. The cause of death was shock and haemorrhage due to rupture of the spleen and stomach.

A verdict of accidental death was returned.

Universities and Colleges

UNIVERSITY OF CAMBRIDGE

Mr. Oliver Louis Zangwill has been appointed Professor of Experimental Psychology in the University from October 1, in succession to Sir Frederic Bartlett, F.R.S. Mr. Zangwill was educated at King's College, Cambridge, graduating B.A. in 1935 and proceeding M.A. in 1939. He has been Senior Lecturer in General Psychology in the University of Oxford since 1948. During the war he was research psychologist to the Brain Injuries Unit at Edinburgh, under the direction of Professor Norman Dott and Sir David Henderson. In 1946 the University of Oxford conferred on him the degree of M.A. The Chair of Experimental Psychology was established in 1931, when Sir Frederic Bartlett became the first occupant. His work has been concerned principally with problems of perception and remembering, and later with the development of the experimental studies of human skill and the problem of work in old age. He was elected F.R.S. in 1932.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

At a meeting of the Council of the College, held on January 10, with Sir Cecil Wakeley, President, in the chair, Mr. Gilbert Causey, who at present is Lecturer in Anatomy and Supervisor of the Museum, University College, London, was appointed as Sir William Collins Professor of Human and Comparative Anatomy at the College.

The Council passed resolutions of condolence on the deaths of Professor Henri Hartmann and Professor D. B. Phemister, both Honorary Fellows of the College.

The following were elected to the Fellowship of the Faculty of Anaesthetists: Dr. S. N. Albert (Beirut), Dr. A. F. Alsop (Oxford), Dr. G. Cousineau (Montreal), Dr. Phyllis M. Edwards (London), Dr. A. C. Forrester (Glasgow), Dr. A. P. Gorham (Bristol), Dr. N. R. James (Melbourne), Dr. J. R. Ritchie (Dunedin).

Diplomas were awarded, jointly with the Royal College of Physicians of London, as follows:

DIPLOMA IN PSYCHOLOGICAL MEDICINE.—C. E. Bagg, J. Cowie, E. T. Downham, R. E. Glennie, Mei-Chen Liu, B. M. Mandelbrote, R. H. Martlew, Marion E. F. Woollaston.

DIPLOMA IN LARYNGOLOGY AND OTOLOGY.—K. D. N. Agrawal, A. Aziz, R. H. Cowling, Than Dok, H. Forer, J. D. Glanville, Beatrice A. J. Gregory, D. F. N. Harrison, W. A. Hopkins, H. M. Jones, Z. A. Khan, P. J. McNicholas, D. V. Maytham, J. R. Page, A. B. N. Rao, M. S. M. Refai, J. Vella, A. L. Wells, G. T. Woods.

DIPLOMA IN MEDICAL RADIODIAGNOSIS.—A. K. Banerji, S. M. Bingurnah, V. H. Bowles, J. Brown, T. Crisp, H. Ferguson, A. M. H. Fisher, H. L. Francis, K. D. Hatfield, H. W. Holland, D. T. Irwin, H. Jacobs, J. B. Jameson, Sheila Kenny, N. A. Lewtas, G. B. Mohanty, P. K. Mookherjee, J. J. Q. Peiris, K. M. Pillai, P. Purcell, Margaret P. Sheridan, G. P. G. Sim, A. G. G. Toomey, D. Urquhart, G. H. Waddington, D. R. Wallace-Jones, J. M. Winn.

DIPLOMA IN MEDICAL RADIOTHERAPY.—Diana M. Brinkley, G. E. Catton, J. H. O. Chance, P. M. C. Corlette, T. J. Deeley, F. M. Hall, P. Haslam, G. A. Hendry, G. Jarratt, G. Lynch, Dorothy Pearson.

DIPLOMA IN ANAESTHETICS.—Janie U. Blacker, A. K. Bose, Margaret L. M. Bridges, Margaret W. Brown, I. S. Bruce, R. W. Buckley, Cicely I. Butterworth, R. G. Cole, J. G. Cranmer, Patricia R. Ford, Elizabeth M. France, I. C. A. D. P. Graham, Edith H. Grundy, Mary J. Hartley, H. B. Houldsworth, J. S. Inkster, M. Junod, P. D. Kelsall, P. Koenig, C. J. Levy, Pauline McArthur, J. Mamak, W. K. Pallister, Edith J. L. Pearce, D. J. Power, J. E. Riding, R. J. Rutherford, A. K. Sen Gupta, Frances Sorrell, Heather Stockdale, J. C. Sumption, G. C. Tandan, M. Tappura, Hildegard H. M. Weisz, Margaret M. Whitaker, P. B. Wolfers.

DIPLOMA IN INDUSTRIAL HEALTH.—H. D. Conway, J. J. du Plessis.

DIPLOMA IN PATHOLOGY.—C. A. K. Bird, N. L. Modi.

DIPLOMA IN OPHTHALMIC MEDICINE AND SURGERY.—D. K. de B. Macdonald.

DIPLOMA OF OPHTHALMOLOGY.—K. D. N. Agrawal.

The following hospitals were recognized under paragraph 23 of the Fellowship regulations: Queen Alexandra Hospital, Army, six house officers (all for 12 months). Queen's Park Hospital, Blackburn, house-surgeon and senior house officer (both for six

months). St. Luke's Hospital, Guildford, surgical registrar for one year, second house-surgeon for six months (additional recognition). Royal East Sussex Hospital, Hastings, two house-surgeons for six months. Buchanan Hospital, St. Leonards-on-Sea, one house-surgeon (urological) for six months. General Hospital, Merton, senior house-surgeon for six months. General Hospital, Middlesbrough, orthopaedic house officer (senior) for six months (additional recognition). Shotley Bridge Hospital, surgical registrar for one year; two house-surgeons for six months. Royal South Hants Hospital, Southampton, registrar and house-surgeon for ear, nose, and throat department (decennial revision). Kent and Sussex Hospital, Tunbridge Wells, confirmation of recognition of post of senior house officer (ear, nose, and throat) previously recognized as registrar.

Vital Statistics

Infectious Diseases During 1951

The incidence of infectious diseases during 1951 was in several ways unusual. Their fluctuations are illustrated in the graphs shown overleaf, where a comparison is made with the highest and lowest weekly figures for 1942–50.

The number of notifications of scarlet fever was the lowest for recent years, while whooping-cough and measles were at the highest level since these diseases were made notifiable. The notifications of whooping-cough exceeded 5,000 cases a week six times during the first quarter of the year. In two weeks during the first quarter over 30,000 cases of measles were notified.

The fall in the incidence of diphtheria was continued during the year. The smallest weekly total of diphtheria during 1951 was 19, compared with 31, 52, 100, and 138 for the minima of the four preceding years. Examination of the trend of diphtheria during the last quarter suggests that the downward trend is being checked and the disease will become stabilized around the present level.

The number of notifications of dysentery reached a very high level, the largest weekly total being 1,672 cases. From the information available it seems that Sonne dysentery accounts for about 95% of the total notifications.

Acute poliomyelitis was much below the level of the two preceding years, but the incidence remains at 3 to 5 times the endemic level before 1947.

The enteric fevers (typhoid and paratyphoid) were more prevalent than in recent years, but the notifications were only about one-third of those during the outbreaks of 1941. The number of deaths from influenza in the great towns was the largest since 1937. The sudden rise in the curve for notifications of puerperal pyrexia and puerperal fever is due to the introduction on August 1, 1951, of a new definition of the disease.

A small feature of the graphs is that, with the exception of those for measles and influenza, they all show a decline in the number of notifications in the last week of the year, which includes the Christmas holiday, from the figure for the previous week; those for measles and influenza show only very small rises.

The number of notifications from the principal epidemic diseases for the past five years is:

England and Wales	1947	1948	1949	1950	1951
Scarlet fever ..	60,524	75,460	71,753	66,852	49,431
Whooping-cough ..	94,241	145,878	102,516	157,714	169,394
Diphtheria ..	10,528	7,903	4,929	2,858	1,969
Measles ..	399,461	396,841	384,361	366,116	615,332
Acute pneumonia ..	34,348	31,096	34,624	30,714	43,181
Meningococcal infections	3,147	1,971	1,586	1,745	1,956
Acute poliomyelitis ..	9,251	2,175	6,850	8,699	3,093
Dysentery	4,179	5,587	4,819	18,135	29,488
Enteric (typhoid and paratyphoid) fevers	880	873	1,138	654	1,438
Great Towns					
Influenza deaths ..	1,774	610	3,091	1,859	7,555

Record Low Infant Mortality Rate

Provisional figures published in the Registrar-General's *Quarterly Return* for the September quarter, 1951, show that the infant mortality and the stillbirth rates are the lowest ever recorded in England and Wales. Deaths of children under 1 year of age numbered 3,998, giving a rate of 23.5 per 1,000 related live births. The previous lowest rate recorded was 24.2 in the same period of last year. Stillbirths registered during the quarter numbered 3,727, giving a rate of 21.7 per 1,000 live and still births, compared with 22.5 in the September quarter of 1950. The previous lowest rate was 22.0 in the September quarter of 1949.

There were 168,028 live births registered during the quarter—a rate of 15.2 per 1,000 population. This is the lowest rate for a September quarter since 1941, when it was 14.0, and continues the decline recorded since the post-war peak of 20.0 in 1947.

Deaths at all ages registered during the quarter numbered 100,090, a rate of 9.1 per 1,000 population. This rate is average for the same quarter over the last five years. The births exceeded the deaths by 67,938. The corresponding increase for the same period of the preceding year was 67,220.

Week Ending January 5

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 1,102, whooping-cough 2,154, diphtheria 45, measles 3,491, acute pneumonia 973, acute poliomyelitis 25, dysentery 295, paratyphoid fever 6, and typhoid fever 2.

Infectious Diseases

In England and Wales during the week ending December 29, 1951, the incidence of infectious diseases decreased. The largest falls in the number of notifications were scarlet fever 457, whooping-cough 417, and dysentery 129.

A fall in the incidence of scarlet fever occurred in every region of the country; the largest declines were Lancashire 46 and London 40. Whooping-cough declined more in the northern section of the country than in the southern. The largest falls were Warwickshire 78 and Yorkshire West Riding 77.

The notifications of diphtheria were 11 fewer than in the preceding week. The chief variations in the local returns were an increase of 4 in Lincolnshire and in Lancashire, and a decrease of 8 in Staffordshire. The largest returns of diphtheria for administrative areas were Grimsby C.B. 5 and Liverpool C.B. 4.

The notifications of measles were 10 more than in the preceding week: the largest of the local variations were a rise of 57 in Staffordshire and a fall of 99 in Cardiganshire.

The number of notifications of acute poliomyelitis was 5 fewer for paralytic and 3 fewer for non-paralytic cases than in the preceding week. The largest returns were Kent 3 and Cheshire 3.

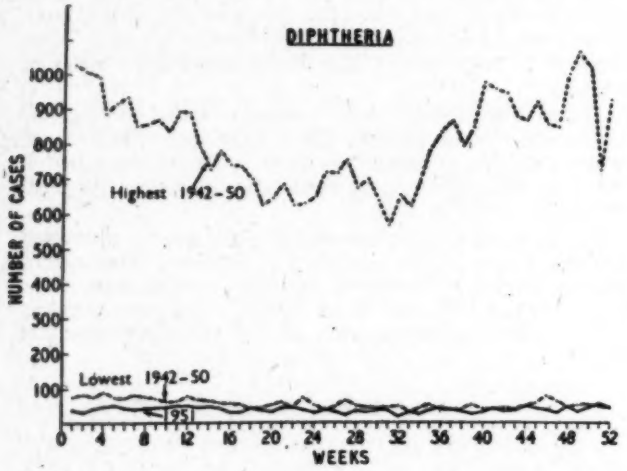
A further 61 cases of dysentery were notified from the outbreak in Norfolk, Norwich C.B. The other large returns were Middlesex 37; Yorkshire West Riding 19; London 17; Bedfordshire 13 (Luton M.B. 12); Leicestershire 13 (Leicester C.B. 10).

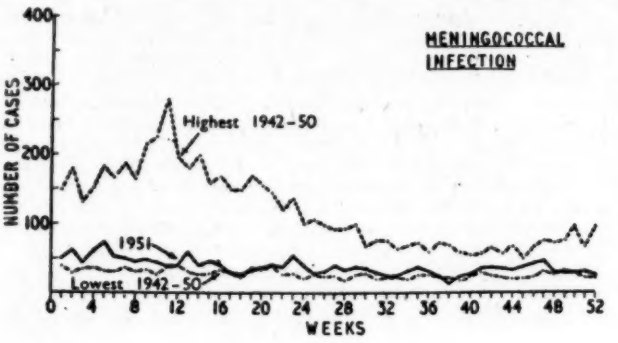
Two large centres of food-poisoning occurred during the week. Buckinghamshire, Wolverton U.D. 133, and Northamptonshire 177 (Towcester R.D. 73, Northampton C.B. 52).

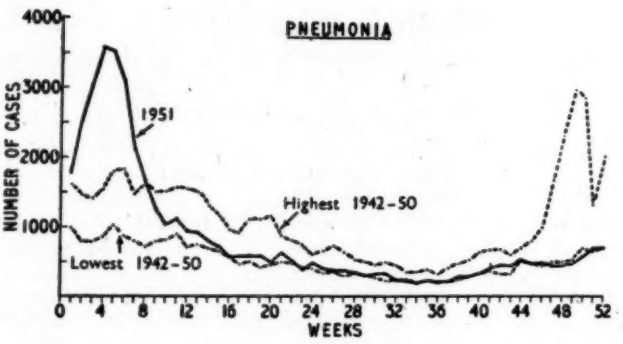
In Scotland a further 38 cases of dysentery were notified in Lanark county, where 101 cases occurred in the preceding week. The other large return in Scotland was 28 notifications in the city of Glasgow.

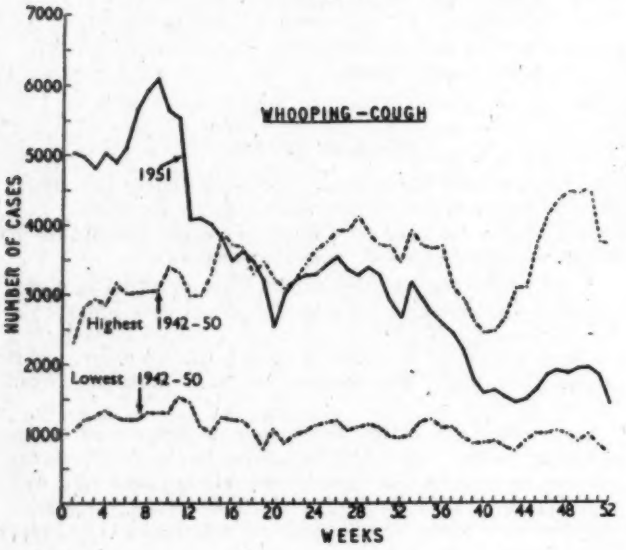
Graphs of Infectious Diseases

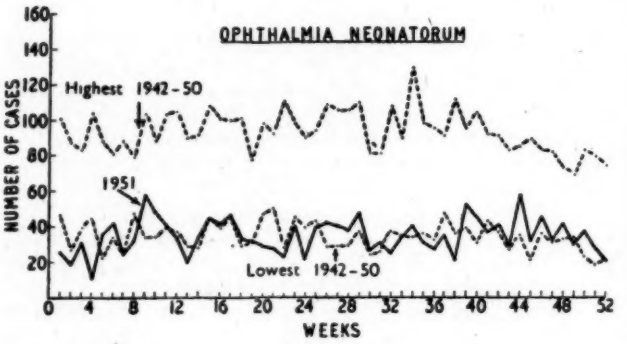
The graphs below show the uncorrected numbers of cases (deaths from influenza) of certain diseases notified weekly in England and Wales. Highest and lowest figures reported during the nine years 1942–50 are shown thus - - - - - - - -, the figures for 1951 thus ————. Except for the curves showing notifications in 1951, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.

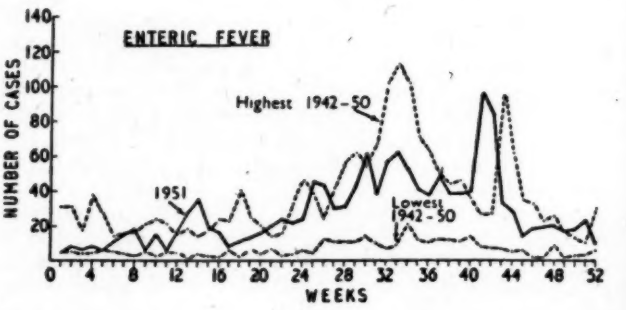


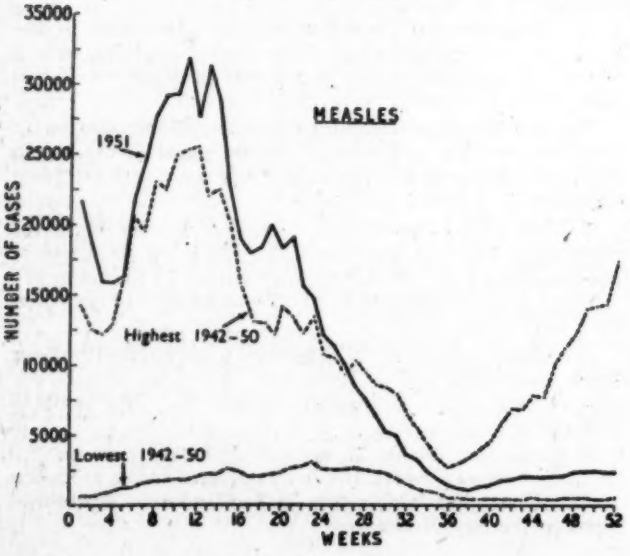


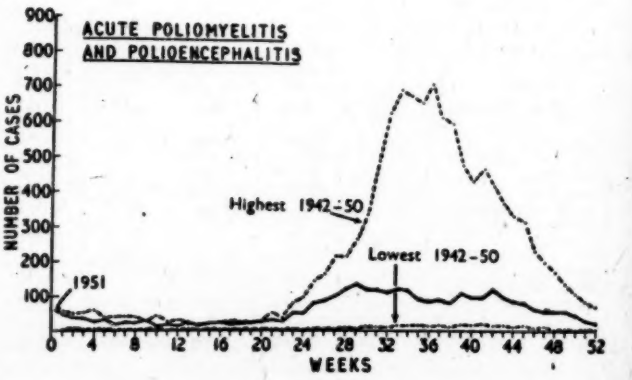


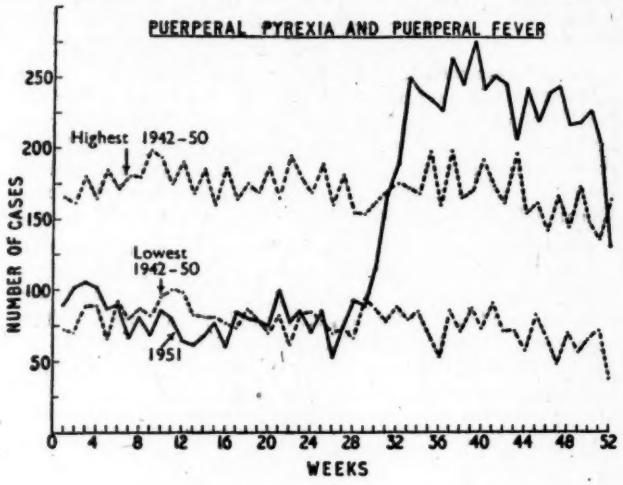


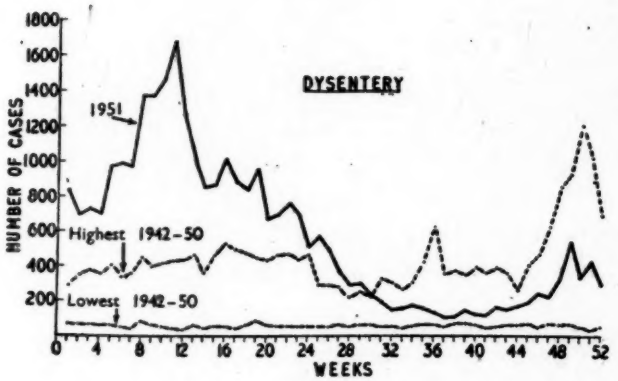


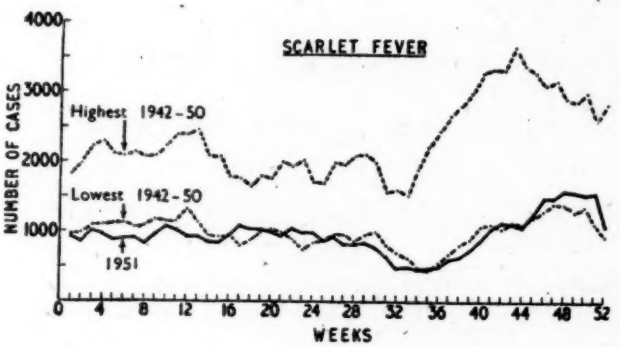


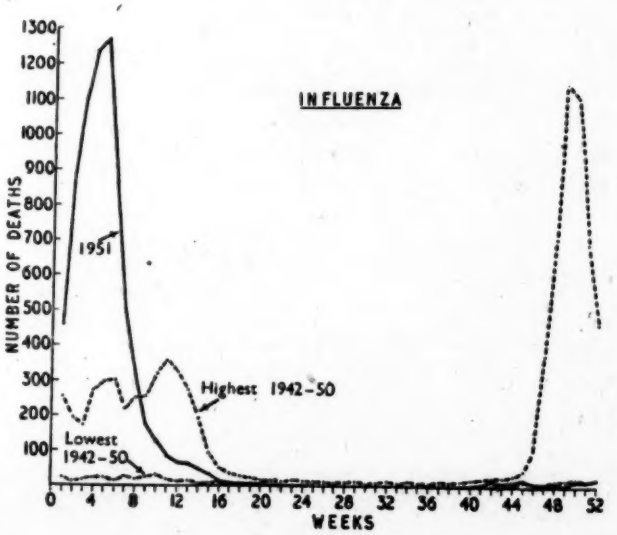












INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending December 29 (No. 52) and corresponding week 1950.

Figures of *cases* are for the countries shown and London administrative county Figures of *deaths* and *births* are for the 126 great towns in England and Wales (London included), London administrative county, the 16 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 13 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1951					1950				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	43	3	13	0	2	41	3	13	5	1
Dysentery	293	17	84	0		691	44	104	5	1
Encephalitis, acute	0	0	0	0		7	0	0	0	
Enteric fever:										
Typhoid	3	2	1	0	0	0	0	0	1	0
Paratyphoid	7	0	1 (B)	1		6	1	0	0	
Food-poisoning	449	7		0		147	26		0	
Infective enteritis or diarrhoea under 2 years				14	9				7	10
Measles*	2,331	19	84	106	42	17,468	1922	102	80	81
Meningococcal infection	26	4	15	1	1	34	2	13	2	3
Ophthalmia neonatorum	20	0	9	0		21	3	10	0	
Pneumonia†	678	30	245	4		962	64	292	6	
Poliomyelitis, acute:										
Paralytic	17	2	} 3	} 0	}	} 53	} 3	} 4	} 0	} 4
Non-paralytic	3	0								
Puerperal fever§	131	21	13	1		38	4	8	4	
Scarlet fever	1,095	72	281	12	41	1,026	62	181	42	52
Tuberculosis:										
Respiratory			142	18				134	26	
Non-respiratory			29	8				28	9	
Whooping-cough	1,402	73	230	60	22	3,690	325	442	25	35

DEATHS in Great Towns	1951					1950				
	Eng. & Wales	Lond.	Scot.	N. Ire	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	1	0	1	0	0	1	0	0	0	0
Dysentery		0		0			0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	12		3	0	2	26		0	2	1
Influenza	22	5	0	0	0	102	8	5	0	1
Measles		0	0	0	0		1	0	0	0
Meningococcal infection		0	1				0	1		
Pneumonia	250	44		7	6	383	48		17	10
Poliomyelitis, acute	0	0			0	5	0			0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	} 131	{ 11	28	10	5	} 199	{ 27	37	8	15
Non-respiratory		0	2	0	0		2	4	1	2
Whooping-cough	0	0	2	1	0	7	4	2	0	1
Deaths 0–1 year	217	30	35	4	9	277	29	50	14	20
Deaths (excluding stillbirths)	5,033	816	612	115	104	7,322	1061	882	138	196
LIVE BIRTHS	5,082	707	804	138	91	5,328	873	841	179	274
STILLBIRTHS	159	25	34			177	25	30		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

Dinner for Lord Horder.—On Monday, January 7, a dinner was given in honour of Lord Horder's 81st birthday by his ex-house-physicians, at the Royal Automobile Club, Pall Mall. Dr. A. F. S. Sladden, as senior house-physician, was in the chair, and the toast of "our teacher," chosen because Lord Horder dedicated his medical notes to his teacher, Samuel Gee, was proposed by Dr. C. A. Hinds Howell, and supported by Sir Hugh Griffiths.

Travelling Fellowships in Ophthalmology and Otology, 1952–3.—The Medical Research Council invite applications for travelling fellowships in ophthalmology and otology for the academic year 1952–3, for which special provision has been made by the Alexander Pigott Wernher Memorial Trustees. Under the terms of the bequest from which these awards are made, the funds are to be applied "towards the prevention and cure of blindness and deafness in the United Kingdom and British Empire and in particular research in connexion therewith by financing medical men and students within the Empire to study methods and practices in all countries of the world." These fellowships are intended for suitably qualified medical graduates who are likely to profit by a period of work in ophthalmology or otology at a centre abroad before taking up positions for higher teaching and research in these branches of medical science. Candidates will be required to submit an outline of their proposals for study or research and to indicate their preference about place of work. The awards will, as a rule, be tenable for one year. The fellowships provide for the payment of stipend, together with an allowance for travelling and incidental expenses. The stipend will ordinarily be at the rate of £650 per annum for a single fellow, and of £900 per annum for a married fellow, subject to appropriate adjustment in the case of fellowships tenable at centres outside the sterling area. Forms of application for these fellowships may be obtained from the Secretary, Medical Research Council, 38, Old Queen Street, London, S.W.1, with whom applications must be lodged by March 31.

Hospital Renamed.—On January 1 the Sheffield Street Hospital, Kingsway, London, W.C.2, became part of the group of teaching hospitals known as St. Peter's and St. Paul's. To mark the change-over the hospital has been renamed St. Philip's. St. Philip's, which has 57 beds, will treat chronic urological cases.

Experimental Parasitology.—The first number of *Experimental Parasitology* appeared recently. This new quarterly journal intends to publish original contributions on experimental physiological, metabolic, biochemical, nutritional, and chemotherapeutic problems of parasites and host–parasite relationships. In addition, a section of the journal will be devoted to reviews covering all aspects of parasitology. *Experimental Parasitology* is published by the Academic Press, Inc., New York, at an annual subscription of $8.00.

American Orthoptic Journal.—The American Academy of Ophthalmology and Otolaryngology has commenced publication of the *American Orthoptic Journal*, which will be issued as an annual supplement to the Academy's *Transactions*, and will contain papers read at its annual meetings.

Emergency Bed Service: Applications and Admissions.—During the seven days ending January 14 the number of applications made by doctors to the London Emergency Bed Service for admission of patients was 1,188, of whom 83.16% were admitted.

Wills.—Dr. William Arnott left £24.000. Bequests included £25 each to the West Riding Medical Charitable Society and the Royal Medical Benevolent Fund. Dr. Frank Constable Porter left £76,398, of which he gave £100 to the Benevolent Fund of the British Dental Association.

COMING EVENTS

Renal Association.—The eighth general meeting of the association will be held at the Ciba Foundation on Wednesday, January 30, at 4.30 p.m. Following the election to honorary membership of Dr. Donald van Slyke and Professor Dérot, papers will be read on the disorders of cellular hydration and experimental pyelonephritis, and Professor Dérot will describe 100 cases of anuria personally treated.

Memorial Service for Lord Addison.—A memorial service for the late Viscount Addison will be held in Westminster Abbey on Wednesday, January 30, at 12.30 p.m. No tickets will be needed by the general public, but seats will be reserved for relatives, Parliamentary colleagues, the Diplomatic Corps, and representatives of public bodies. Inquiries regarding arrangements should be made to Mr. Carol Johnson, Parliamentary Labour Party, Palace of Westminster, London, S.W.1.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Friday

UNIVERSITY COLLEGE, LONDON: FACULTY OF MEDICAL SCIENCES.—At Anatomy Theatre, Gower Street, London, W.C., January 18, 4.30 p.m., "*The Hypothalamus and the Neuro-hypophysis*," public lecture by Professor W. Bargmann (Kiel University).

Monday

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—January 21, 5 p.m., "*Refraction Work in the Aged. Prescription and Fitting of Glasses*," by Dr. T. H. Whittington.

Tuesday

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, W.C., January 22, 5.30 p.m., "*Involuntary Nervous System*," by Professor G. L. Brown, F.R.S.

EUGENICS SOCIETY.—At Royal Society, Burlington House, Piccadilly, London, W., January 22, 5.30 p.m., "*Recording Human Constitution*," by Dr. R. W. Parnell.

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—January 22, 5.30 p.m., "*Hysteria Cutis*," by Dr. W. J. O'Donovan.

LONDON COUNTY MEDICAL SOCIETY.—At Talbot Restaurant, London Wall, E.C., January 22, 7 for 7.30 p.m., annual general meeting and dinner.

ST. ANDREWS UNIVERSITY.—At Physics Lecture Theatre, Materia Medica Department, Medical School, Small's Wynd, Dundee, January 22, 5 p.m., "*Some Recent Developments in the Study of the Biological Actions of Ionizing Radiations*," by Dr. L. H. Gray, Ph.D.

Wednesday

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—January 23, 5.30 p.m., "*Mycology—Moniliasis: Torulosis*," by Dr. R. W. Riddell.

INSTITUTE OF UROLOGY.—At St. Paul's Hospital, Endell Street, London, W.C., January 23, 4.30 for 5 p.m., "*Tuberculosis of the Renal Tract*," by Mr. F. R. Kilpatrick.

NORTH-EAST METROPOLITAN REGIONAL TUBERCULOSIS SOCIETY.—At London Chest Hospital, Victoria Park, E., January 23, 3 p.m., "*Congenital Abnormalities of the Chest*," by Mr. T. Holmes Sellors. Pathological demonstration by Dr. K. F. W. Hinson.

SOCIETY OF CHEMICAL INDUSTRY.—At Burlington House, Piccadilly, London, W., January 23, 6.30 p.m., joint meeting of Nutrition Panel—Food Group and Oils and Fats Group. "*The Digestibility of Fat*," by Dr. H. Wilkinson, Ph.D., F.R.I.C.

Thursday

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, W.C., January 24, 5.30 p.m., "*Involuntary Nervous System*," by Professor G. L. Brown, F.R.S.

●INSTITUTE OF CHILD HEALTH, Hospital for Sick Children, Great Ormond Street, London, W.C.—January 24, 5 p.m., "*Surgery of the Brain in Childhood*," by Professor H. Cairns.

LIVERPOOL MEDICAL INSTITUTION, 114, Mount Pleasant, Liverpool.—January 24, 8 p.m., pathological meeting.

MEDICO-LEGAL SOCIETY.—At 26, Portland Place, London, W., January 24, 8.15 p.m., "*Testamentary Capacity*," by Mr. W. Latey, K.C.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner, London, S.W.—January 24, 4.30 p.m., lecture-demonstration in neurology.

ST. JOHN'S HOSPITAL DERMATOLOGICAL SOCIETY, Lisle Street, Leicester Square, London, W.C.—January 24, 4.15 p.m., demonstration and discussion of clinical cases.

Friday

CAMBRIDGE MEDICAL SOCIETY.—January 25, "*Newer Developments in Radiotherapy*," by Professor J. S. Mitchell.

EDINBURGH UNIVERSITY: FACULTY OF MEDICINE.—At Anatomy Lecture Theatre, University New Buildings, Teviot Place, Edinburgh, January 25, 5 p.m., "*Serum Cholesterol, 'Giant Molecules,' and Atherosclerosis*," Macarthur Postgraduate Lecture by Professor Ancel Keys, M.A., Ph.D. (University of Minnesota).

INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—January 25, 5.30 p.m., "*Xanthoma and Necrobiosis Lipoidica*," by Dr. P. D. Samman. Clinical demonstration.

INSTITUTE OF DISEASES OF THE CHEST AND INSTITUTE OF CARDIOLOGY.—At London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, W.C., January 25, 5.30 p.m., "*Anaesthesia for Cardiac Surgery*," by Dr. B. G. B. Lucas.

MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES, 11, Chandos Street, London, W.—January 25, 7.30 p.m., general meeting "*Possible Applications of A.C.T.H. and Cortisone in Syphilis*," discussion to be opened by Dr. Gordon Horne.

OXFORD UNIVERSITY.—At Magdalen College, Oxford, January 25, 5 p.m., "*The Neurophysiological Basis of Mind*," Wayneflete Lecture by Professor J. C. Eccles, F.R.S.

ROYAL MEDICAL SOCIETY, 7, Melbourne Place, Edinburgh.—January 25, 8 p.m., "*Human Faces*," by Mr. A. R. Isaac.

ROYAL SANITARY INSTITUTE.—At Public Hall, Lune Street, Preston, January 25, 10 a.m., papers: "*Tuberculosis Control, with Some Comments on Lung Cancer*," by Dr. W. Griffel; "*The Changing Role of the Health Visitor*," by Miss E. W. Sowerby, S.R.N., S.C.M.; "*The Influence of Lighting Developments on Health and Safety*," by Dr. J. N. Aldington, Ph.D.; 2 p.m., visits will be made.

Saturday

SOCIETY OF PUBLIC ANALYSTS: NORTH OF ENGLAND SECTION.—At Engineers' Club, Albert Square, Manchester, January 26, 2 p.m., 27th annual general meeting. An ordinary meeting will follow. "*The Use of Laboratory Animals as Analytical Reagents*," by Mr. A. L. Bacharach, M.A., F.R.I.C.

APPOINTMENTS

BRANNEN, IAN CAMERON, M.B., Ch.B., Registrar, Royal Northern Infirmary, Inverness.

HOSPITAL FOR SICK CHILDREN, Great Ormond Street, London, W.C.—*Senior Surgical Registrar (Senior Registrar Grade)*, Ambrose Jolleys, M.B., Ch.B., F.R.C.S. *Resident Anaesthetic Registrar (Registrar Grade)*, W. A. D. Combe, M.R.C.S., L.R.C.P. *Assistant Resident Medical Officer (Senior House Officer Grade) at Tadworth*, Elizabeth M. C. Dyke, B.M., B.Ch., D.C.H. *House-physicians (Senior House Officer Grade)*, Kenneth Simpson, M.B., B.S., M.R.C.P., and M. J. Simpkiss, M.B., Ch.B., M.R.C.P. *House-surgeon (Senior House Officer Grade)*, M. R. Kliman, M.D., F.R.C.S.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Beynon.—On November 28, 1951, at Hong Kong, to Dr. Peggy Beynon (formerly Thomas), wife of Major Glanley Beynon, S.C.F., a daughter.

Hatcher.—On November 13, 1951, to Joan (formerly Tanner), M.B., B.S., wife of Mr Edmund Hatcher, a daughter—Susan Elizabeth Jane.

Judson.—On January 4, 1952, at Hull, to Helen (formerly Atwell), wife of Dr David Judson, a daughter.

Kelsall.—On January 6, 1952, in London, to Margaret (formerly Miller), wife of Dr. A. R. Kelsall, a daughter.

MARRIAGES

Slattery—Kelly.—On January 10, 1952, at St. Saviour's Church, Totland, Isle of Wight, John Anthony Slattery, M.B., B.S., of Canonbury, London, N., to Zoë Taschereau Kelly, M.B., B.S., D.C.H., of Freshwater, Isle of Wight.

DEATHS

Cargill.—On December 9, 1951, at South Elmsall, Yorks, Diana Pamela Mary Sylvester Cargill, L.R.C.P.&S.Ed., L.R.F.P.S.

Clark.—On January 5, 1952, at The Vinery, Wellington, Hereford, Henry Colbatch Clark, M.R.C.S., L.R.C.P.

Cockburn.—On January 12, 1952, at Southcliffe, Chalfont St. Peter, Bucks, Robert Pitcairn Cockburn, M.D., aged 86.

Dobson.—On January 9, 1952, at Craiglands Hydro Hotel, Ilkley, Yorks, Maurice Rowland Dobson, O.B.E., M.B., B.S., aged 73.

Dodson.—On January 2, 1952, Eleanor Isabel Dodson, M.D., of London, S.E., formerly of Multan, India.

Greene.—On January 7, 1952, in a nursing-home, Jersey, George Watters Greene, M.D., D.P.M., aged 74.

Gregory.—On January 12, 1952, in London, Hazel Haward Chodak Gregory (formerly Cuthbert), M.D., F.R.C.P.

Greig.—On January 6, 1952, at 23, Townsend Place, Kirkcaldy, John Isdale Greig, M.B.E., M.B., Ch.B.

Grunhut.—On January 10, 1952, Jozef Grunhut, M.D., aged 51.

Maddock.—On January 6, 1952, Edward Cecil Gordon Maddock, C.I.E., M.D., F.R.C.S.Ed., D.P.H., D.T.M., Lieutenant-Colonel, I.M.S., retired, of Wardon Lodge, Sunningdale, Berks.

Moiser.—On January 6, 1952, at 15, Watercall Avenue, Coventry, Lionel Henry Moiser, M.B.

Nicklin.—On January 8, 1952, at Luanshya, Northern Rhodesia, Reginald Nicklin, M.B., Ch.B.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Stains on Doctors' Clothes

Q.—*What is the best way of removing stains on clothes due to (a) flavine, (b) iodine, and (c) blood?*

A.—*Flavine Stains.*—Treat the stain with dilute hydrochloric acid or with dilute sulphurous acid, and then wash.

Iodine Stains.—These can readily be removed by sponging with a solution of sodium thiosulphate (photographic hypo). Dilute ammonia can also be used.

Blood Stains.—Fresh stains may be removed by sponging with cold or slightly warm (*not* hot) water, followed, if necessary, by the application of solution of hydrogen peroxide. The following methods are suggested in *Pharmaceutical Formulas*, published by the *Chemist & Druggist*—"In the case of delicate materials the following procedure is often successful: Prepare a paste of rice starch and water which is applied to the stain and allowed to dry on. Other methods consist in the application of a solution of borax, dilute solution of ammonia, tincture of quillaia, soap spirit, or solution of hydrogen peroxide followed by dilute solution of ammonia. A solution of tribasic sodium phosphate is also recommended for removing blood stains, and in some instances glacial acetic acid may be successful. In the case of old stains, these should first be thoroughly moistened with warm water, preferably with a slight addition of glycerin. In these cases the stains often yield to treatment with a concentrated solution of chloral hydrate (75%), after moistening the stain with dilute acetic acid. In recalcitrant cases of old blood stains a solution of pepsin, 4 gr. (0.25 g.); dilute hydrochloric acid, 20 min. (1.2 ml.); distilled water, 3 oz. (85 ml.) may prove successful in removing the albumin, followed by the application of one of the above-mentioned agents to remove the discoloration."

Hypnosis and Asthma

Q.—*Is there any evidence that hypnotic treatment can benefit sufferers from chronic asthma? What might be its dangers, particularly with children?*

A.—There is no doubt that very small factors, some of them psychological, can precipitate or inhibit attacks in a chronic asthmatic. At the end of a period of frequent attacks the patient may have acquired a faulty respiratory rhythm and posture which, through fear of future attacks, do not return at once to normal in a negative phase. At this stage, in children, education in relaxation of the respiratory muscles and in expansion of the bases can be aided by a method of suggestion such as hypnosis, which may for the time being eliminate this fear. This use of hypnosis is comparable with its use in stammering, where enduring improvement can be expected only if the child learns to relax apart from the hypnotic session. Even where a pre-existing asthma is used by the child as a purposive "functional" dyspnoea, a dramatic result should not prevent a search for causes of the underlying maladjustment, allergic, infective, or psychological.

A successful frontal attack on the asthma by means of hypnosis has often been reported, but usually where attacks are occasional. Many chronic asthmatics will report improvement because they cannot always tell the difference between an actual attack and wheeziness. They can easily be induced to feel that no attack is present and that none is pending.

The risks are those of any hypnotic treatment in children: that unless the children are carefully handled they may

develop a habit of going into unnecessarily deep hypnosis and of having anaesthesia, disturbance of memory, or tetany which may continue in the waking state.

Scrotal Retention Cysts

Q.—*A male infant of 7 months has three or four white spots in the skin of the median raphe of the penis at its junction with the scrotum. The spots are about 2 mm. in diameter and are just under the cuticle; they appear to cause some irritation. What are they? What treatment is advised?*

A.—It would appear from the description given that these spots are small retention cysts similar to the "epithelial pearls" or "Bohn's nodules" seen in the midline of the hard palate in most newborn infants and due to overgrowth of the epidermis covering over the mouths of the glands. The spots will disappear spontaneously. No treatment is necessary except regular cleansing of the parts.

Salt and Boils

Q.—*Could an excessive intake of salt have any bearing on the development of recurrent axillary boils? A patient with this complaint takes a good deal of salt with his food, and also during his work. His job is to service water softeners and recharge them with salt; during the process he has to taste for brine until it is no longer noticeable in the water.*

A.—There is no evidence that an excessive intake of salt could have any bearing upon the development of recurrent axillary boils.

Enuresis

Q.—*Where can I find information on the investigation and treatment of enuresis?*

A.—On p. 185 of the book "*Any Questions?*" The book can be obtained for 7s. 6d. (postage 6d.) from the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1.

Hazards of Ethyl Acetate and Toluene

Q.—*Until recently ethyl acetate has been the solvent for lacquers in a factory where I am the doctor. Now 10% toluene is being added to the ethyl acetate to diminish the risk of fire, and there is a likelihood that the concentration of toluene in the solvent will soon be raised to 40%. Until the toluene was added, there had been no complaints of skin irritation from those handling either the solvent or the lacquer; now the men are complaining of burning and irritation when their hands and arms are exposed to the ethyl acetate–toluene mixture. (1) What are the known occupational hazards from ethyl acetate and toluene? (2) What can be done to reduce any such hazard? Are barrier creams, for instance, effective?*

A.—(1) Ethyl acetate is an irritant and is mildly narcotic. In acute poisoning the irritant effects—e.g., acute pulmonary oedema—predominate. No definite chronic effects have been described. The maximum permissible concentration is 400 parts per million.

Toluene is a narcotic, and the general consensus of opinion is that it is free from the undesirable chronic effects of benzene—namely, the liability to produce agranulocytosis and aplastic anaemia. But it must be remembered that toluene may contain benzene as an impurity. The permissible concentration is 200 p.p.m. Clinical accounts of workers exposed to toluene will be found in *J. Amer. med. Ass.*, 1942, **118**, 573 and 579; 1943, **123**, 1106. They suggest that in concentrations as high as 200 p.p.m. some incoordination of fine movements may develop.

(2) The value of barrier creams in protecting the skin from mineral oil has been examined, and in general they were without effect (*Brit. J. industr. Med.*, 1948, **5**, 204). They are probably even less effective against substances such as toluene. It will obviously be necessary, therefore, to arrange for physical protection of the skin in the factory described.

NOTES AND COMMENTS

Paroxysmal Tachycardia in Pregnancy.—Dr. E. D. KERR (High Wycombe, Bucks) writes: The "Any Questions?" section of the *Journal* (December 15, 1951, p. 1473) advises the administration of digitalis for the treatment of paroxysmal tachycardia occurring in pregnant women. There are theoretical and statistical reasons for believing that digitalis may cause foetal death. Digitalis, being a glucoside, could easily pass the placental barrier in a concentration sufficient to poison the heart of a foetus. The effect of digitalis on the foetal heart would presumably be the same as the effect on an adult heart, and a large dose would cause heart block and ventricular fibrillation. The foetal mortality rate when heart disease of the mother is present in pregnancy bears a direct relationship to the onset in the mother of cardiac decompensation and auricular fibrillation, especially the latter. The attendant impairment of circulation, with the coexisting anoxaemia, is generally considered to be the cause of foetal death, but anoxaemia is often not present to any marked extent, and other factors must be involved. One of these could be the effect of digitalis, since the drug is nearly always administered to these cases. In pregnancy the administration of digitalis is on many occasions a life-saving therapeutic measure for the mother, but it is not justifiable to employ digitalis in the treatment of paroxysmal tachycardia, since its beneficial effect on the mother may be minimal, but its detrimental effect on the foetus may be lethal.

OUR EXPERT writes: While it is possible on theoretical grounds for digitalis to have toxic effects on the foetal heart, there is no doubt of its great value in treating heart failure of pregnancy. The beneficial effect on the mother increases the chances of a live birth, and digitalis should invariably be used in the presence of heart failure, whether or not this is associated with paroxysmal tachycardia.

Dr. A. B. UNWIN (London, S.W.1) writes: In my experience attacks of paroxysmal tachycardia in persons with clinically normal hearts have been associated with excessive gaseous distension of the stomach or large intestine, cessation of an attack often being associated with the bringing up of wind. Presumably the heart is irritated by displacement upwards due to pressure from below the diaphragm. During pregnancy two possible factors could be involved. First, transmitted pressure due to the enlarging uterus, and, secondly, the effects of pregnancy hormones on the intestinal muscle tone, which tend to allow dilatation with retention of gas. An attack is usually begun as a result of a sudden movement or effort and the patient can feel it as it starts. A simple measure often effective in cutting short an attack is to take a deep breath and hold it in full inspiration; the pressure in the chest is then raised by making an effort to expel the air with the glottis closed. Other methods sometimes recommended, such as pressure over the carotid sinus or pressing the eyeballs, do not appear very effective in practice. All tight belts and corsets should be removed from the abdomen and a hot drink sipped to assist in the relief of gas from the stomach. The general treatment should be directed towards the dyspepsia The most important single factor in the causation of abdominal distension with gas is anxiety and emotional stress, and a good general practitioner should be of help in this respect. Phenobarbitone, gr. ½ (32 mg.) three times a day before meals, should be prescribed. Attention to diet and a warning against overeating should be given, and a glass of early-morning salts taken to prevent constipation and to assist in the general tone of the intestine and gall-bladder. Should a severe case fail to respond to these simple measures, then "prostigmin" may presumably be worthy of trial.

OUR EXPERT writes: The simple measures outlined above may be beneficial, but prostigmin is not likely to be effective unless given in near toxic doses, and should only be used after a trial of quinidine and procaine amide. Anxiety is more likely to be secondary to the attacks of paroxysmal tachycardia than the cause of them. Aerophagy and subsequent eructation are also secondary to the attacks of arrhythmia rather than the cause of them: the same symptoms may be present in patients with precordial or epigastric discomfort from other causes.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 4499 TELEGRAMS: *Aitiology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.
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